Printy 5/13/04

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=> fil reg
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=> d ide can l7

L7   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   108736-35-2  REGISTRY
CN   L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-
     tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2→7)-disulfide
     (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1,2-Dithia-5,8,11,14,17-pentaazacycloeicosane, cyclic peptide deriv.
OTHER NAMES:
CN   1: PN: WO0006185 PAGE: 8 claimed protein
CN   2: PN: EP1118336 SEQID: 2 claimed protein
CN   37: PN: WO0198330 PAGE: 15 unclaimed sequence
CN   3: PN: WO0006185 PAGE: 8 claimed protein
CN   48: PN: US6268342 SEQID: 53 claimed protein
CN   Angiopeptin
CN   Autogel
CN   BIM 23014
CN   DC 13-116
CN   Ipstyl
CN   Lanreotide
CN   Lanreotide Autogel
FS   PROTEIN SEQUENCE; STEREOSEARCH
DR   123369-01-7, 118992-92-0
MF   C54 H69 N11 O10 S2
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, ADISNEWS, BIOBUSINESS, BIOSIS, CA, CANCERLIT,
       CAPLUS, CBNB, CHEMCATS, DDFU, DRUGU, IMSDRUGNEWS, IMSPATENTS,
       IMSRESEARCH, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, TOXCENTER, USAN,
       USPAT2, USPATFULL
         (*File contains numerically searchable property data)

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
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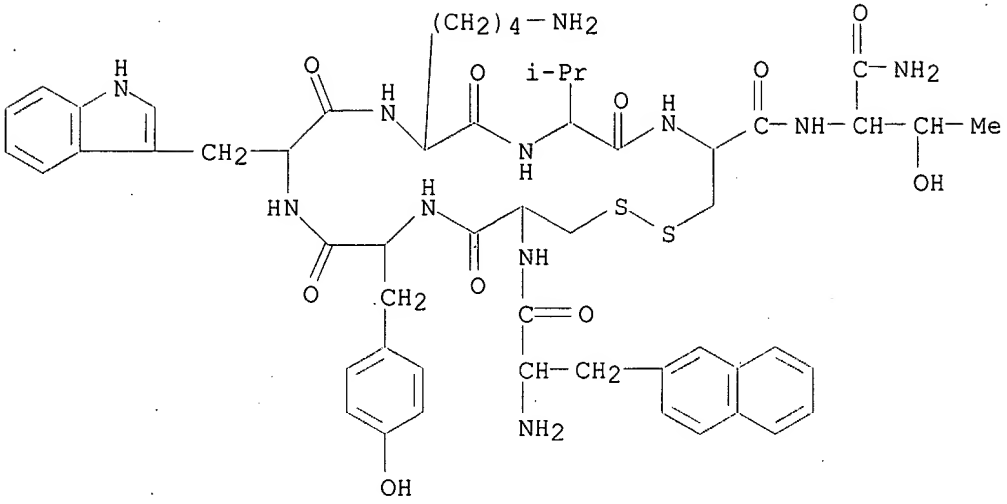

319 REFERENCES IN FILE CA (1907 TO DATE)
20 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
320 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:13165

REFERENCE 2: 140:983

REFERENCE 3: 140:819

REFERENCE 4: 139:399770

REFERENCE 5: 139:391058

REFERENCE 6: 139:375363

REFERENCE 7: 139:375358

REFERENCE 8: 139:359237

REFERENCE 9: 139:333384

REFERENCE 10: 139:316206

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(FILE 'HOME' ENTERED AT 07:39:34 ON 11 FEB 2004)
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L1 1 S WO98-EP2999/AP,PRN
SEL RN

FILE 'REGISTRY' ENTERED AT 07:40:01 ON 11 FEB 2004
L2 118 S E1-E118
L3 15 S L2 AND C6-C6/ES
L4 13 S L3 AND S/ELS
L5 11 S L4 AND 8/SQL
L6 4 S L5 NOT PHENYLALAN?
SEL RN 4
L7 1 S E119

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     FILE 'HCAPLUS' ENTERED AT 07:48:50 ON 11 FEB 2004
L8          320 S L7
L9          390 S ANGIOPEPTIN# OR ANGIO PEPTIN# OR BIM23014 OR BIM()(23014 OR 2
L10         417 S L8,L9
                E CAWTHORNE M/AU
L11         140 S E3-E7
                E LIU Y/AU
L12        1646 S E3,E21
                E LIU YONG/AU
L13         787 S E3,E41,E42
                E LIU YONGL/AU
L14          13 S E10,E11
                E SENNITT M/AU
L15          31 S E4-E6
                E SENNIT M/AU
                E SENIT M/AU
L16           4 S L10 AND L11-L15
L17         181 S L10 AND (PY<=1997 OR PRY<=1997 OR AY<=1997)
                E BODY WEIGHT/CT
L18       15919 S E3-E5
                E E3+ALL
L19       15919 S E2
                E E8+ALL
L20       18476 S E2+NT
                E E7+ALL
L21        4293 S E4,E3+NT
                E E8+ALL
L22        2009 S E4,E3+NT
                E E10+ALL
L23       14601 S E2+NT
                E E7+ALL
L24         422 S E3+NT
                E OBESITY/CT
L25       18159 S E3-E7
                E E3+ALL
                E E6+ALL
L26       37600 S E4+NT
                E E13+ALL
                E E11+ALL
L27       29514 S E1
                E E6+ALL
L28        4622 S E3,E2
L29           2 S L17 AND L18-L28
L30           8 S L10 AND L18-L28
L31          10 S L16,L29-L30
L32           2 S L17 AND BODY()(WEIGHT OR WT OR MASS)
L33           0 S L17 AND BODY()FAT
L34           2 S L17 AND (WEIGHT OR WT)(L)(GAIN? OR LOSS OR LOSE OR LOSING)
L35           4 S L17 AND (WEIGHT OR WT)(L)REDUC?
L36           5 S L32-L35
L37           3 S L36 NOT L31
                SEL DN AN L37 2
L38           1 S E1-E3 AND L37
L39           2 S L37 NOT L38
L40           3 S L36 NOT L39
L41          11 S L31,L40
L42          11 S L41 AND L1,L8-L41
L43           2 S L17 AND (?OBESI? OR ?OBESE?)
L44          11 S L42,L43
                E APPETITE/CT
L45           1 S L10 AND E3-E23
                E E3+ALL
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L46           1 S L10 AND E2+NT
                E APPETITE/CT
                E E21+ALL
                E E2+ALL
                E E2+ALL
                E EAT/CT
                E E6+ALL
                E ANOREXIA/CT
                E E3+ALL
L47           1 S L10 AND E3,E2+NT
                E BULIM/CT
                E E5+ALL
L48           1 S L10 AND E2
L49           1 S L10 AND (BULIMI? OR ANOREX?)
L50           1 S L45-L49
L51          11 S L44,L50

     FILE 'REGISTRY' ENTERED AT 08:05:20 ON 11 FEB 2004

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FILE LAST UPDATED: 10 Feb 2004  (20040210/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d l51 all hitstr tot

L51  ANSWER 1 OF 11  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:670168  HCAPLUS
DN   140:819
ED   Entered STN:  28 Aug 2003
TI   The therapeutic potential of somatostatin receptor ligands in the
     treatment of obesity and diabetes
AU   Boehm, Bernhard O.
CS   Division of Endocrinology, Ulm University, Ulm, 89070, Germany
SO   Expert Opinion on Investigational Drugs (2003), 12(9), 1501-1509
     CODEN: EOIDER; ISSN: 1354-3784
PB   Ashley Publications Ltd.
DT   Journal; General Review
LA   English
CC   2-0 (Mammalian Hormones)
     Section cross-reference(s): 14, 63
AB   A review.  Since the development of synthetic somatostatin analogs,
     several therapeutic applications for somatostatin receptor agonist mols.
     have been defined.  Established applications for somatostatin analog
```

treatment include pituitary tumors (growth hormone and TSH-secreting adenomas), neuroendocrine tumors of the pancreas and gastrointestinal tract (so-called carcinoid tumors, vasoactive intestinal tumors) and gastroenterol. conditions (pancreatitis, gastrointestinal bleedings, refractory diarrheas, pancreatic and intestinal fistulas, diarrhea in AIDS). Further areas for development of somatostatin analog therapy include obesity, polycystic ovary syndrome and diabetes mellitus, dysmetabolic conditions that are often interrelated. The challenge for the future will be to transform results from clin. trials conducted in heterogeneous clin. situations into novel options of somatostatin analog use. Since obesity and diabetes mellitus both are disorders of marked heterogeneity, the subgroup of patients that will benefit most from somatostatin analog treatment has yet to be defined. In addition, the development of more universal ligands covering all of the known somatostatin receptor mols. as well as receptor subtype specific agents is currently underway. The establishment of slow-release depot formulations of octreotide and **lanreotide** has already provided a more acceptable and consistent delivery mechanism. Use of biodegradable polymer microsphere formulations provides the basis for the development of novel applications, which include hyperinsulinemia, obesity and polycystic ovary syndrome as components of the dysmetabolic syndrome. The most developed thus far is the use of octreotide in hyperinsulinemic forms of obesity and in distinct stages of diabetic retinopathy.

ST review somatostatin receptor ligand obesity diabetes therapy

IT Eye, disease
(diabetic retinopathy; somatostatin receptor ligands therapeutic potential in treatment of obesity and diabetes)

IT Diabetes mellitus
(non-insulin-dependent; somatostatin receptor ligands therapeutic potential in treatment of obesity and diabetes)

IT Ovary, disease
(polycystic; somatostatin receptor ligands therapeutic potential in treatment of obesity and diabetes)

IT Antidiabetic agents
Antiobesity agents
Drug delivery systems
Human
Obesity
(somatostatin receptor ligands therapeutic potential in treatment of obesity and diabetes)

IT Somatostatin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(somatostatin receptor ligands therapeutic potential in treatment of obesity and diabetes)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperinsulinemia; somatostatin receptor ligands therapeutic potential in treatment of obesity and diabetes)

IT 51110-01-1, Somatostatin-14
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(somatostatin receptor ligands therapeutic potential in treatment of obesity and diabetes)

IT 51110-01-1D, Somatostatin-14, analogs 83150-76-9, Octreotide
108736-35-2, Lanreotide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(somatostatin receptor ligands therapeutic potential in treatment of obesity and diabetes)

RE.CNT 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Adamis, A; Am J Ophthalmol 1994, V118, P445 MEDLINE
(2) Aiello, L; N Engl J Med 1994, V331, P1480 MEDLINE
(3) Alberti, K; Diabet Med 1998, V15, P539 MEDLINE

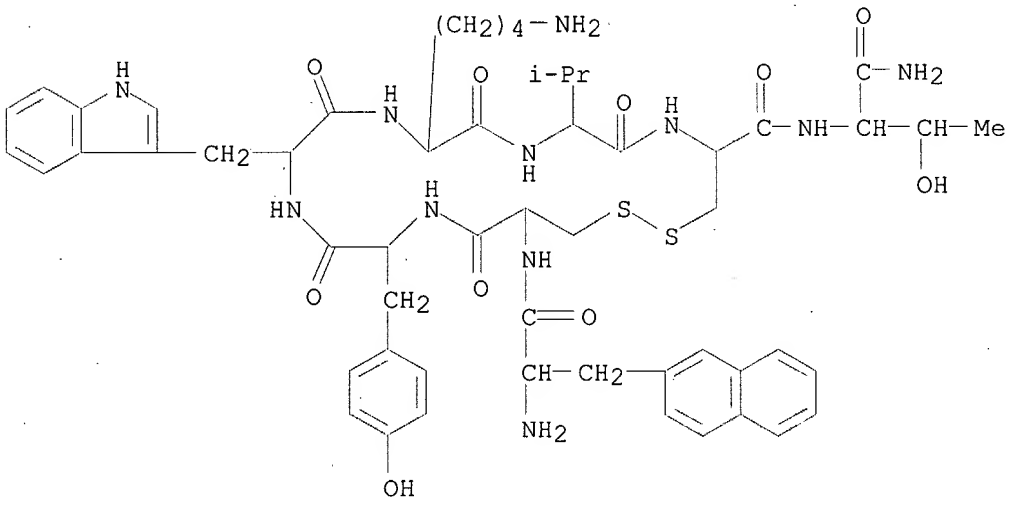
(4) Boehm, B; Baillieres Best Pract Res Clin Gastroenterol 2002, V16, P493 HCAPLUS
(5) Boehm, B; Diabetologia 2003, V46, P394 HCAPLUS
(6) Boehm, B; Horm Metab Res 2001, V33, P300 HCAPLUS
(7) Boehm, B; Octreotide:the Next Decade 1999, P241 HCAPLUS
(8) Bonadonna, R; Metabolism 1990, V39, P452 HCAPLUS
(9) Bouck, N; Trends Mol Med 2002, V8, P330 HCAPLUS
(10) Bray, G; Medicine 1975, V54, P301 MEDLINE
(11) Bray, G; Nature 1978, V274, P900 MEDLINE
(12) Bray, G; Nature 2000, V404, P672 HCAPLUS
(13) Calle, E; N Engl J Med 1999, V341, P1097 MEDLINE
(14) Calle, E; N Engl J Med 2003, V348, P1625
(15) Campfield, L; Obesity Res 1995, V3, P591S HCAPLUS
(16) Chaturvedi, N; Diabetes Care 2001, V24, P284 MEDLINE
(17) Ciotta, L; Hum Reprod 1999, V14, P2951 HCAPLUS
(18) Clemens, A; Metabolism 1999, V48, P1236 HCAPLUS
(19) Fernandez-Real, J; Endocrine Rev 2003, V24, P278 HCAPLUS
(20) Flyvbjerg, A; Diabet Med 1970, V7, P387
(21) Goni, M; Am J Reprod Immunol 1994, V31, P104 MEDLINE
(22) Grant, M; Diabetes Care 2000, V23, P504 HCAPLUS
(23) Grant, M; Drugs Today 2002, V38, P783 HCAPLUS
(24) Groop, L; J Intern Med 2001, V250, P105 HCAPLUS
(25) Haffner, S; Diabetes 1996, V45, P742 HCAPLUS
(26) Jeanrenaud, B; Diabetologie 1985, V28, P502 HCAPLUS
(27) Klein, R; Textbook of Diabetes (2nd edn) 1997, V44, P1
(28) Knutson, V; J Biol Chem 1991, V266, P15656 HCAPLUS
(29) Kohner, E; Br Med J 1993, V307, P1195 MEDLINE
(30) Kondo, T; J Clin Invest 2003, V111, P1835 HCAPLUS
(31) Kopelman, P; Nature 2000, V404, P635 HCAPLUS
(32) Korner, J; J Clin Invest 2003, V111, P565 HCAPLUS
(33) Kosake, K; Diabet Med 1996, V13, PS109
(34) Kuijpers, R; N Engl J Med 1998, V338, P624 MEDLINE
(35) Lamberts, S; N Engl J Med 1996, V334, P246 HCAPLUS
(36) Lamberts, S; Trends Endocrinol Metabol 2001, V13, P451
(37) Legro, R; Endocrine Rev 2003, V24, P302
(38) Lestunff, C; Diabetes 1994, V43, P696 HCAPLUS
(39) Lillioja, S; J Clin Endocrinol Metab 1991, V73, P866 MEDLINE
(40) Lustig, R; Endocrinol Metab Clin North Am 2001, V30, P765 HCAPLUS
(41) Lustig, R; Endocrinologist 2002, V12, P210
(42) Lustig, R; J Clin Endocrinol Metab 2003, V88, P2586 HCAPLUS
(43) Lustig, R; J Pediatrics 1999, V135, P162 HCAPLUS
(44) Marin, P; Metabolism 1988, V36, P1154
(45) Mokdad, A; JAMA 1999, V282, P1519 MEDLINE
(46) O'Rahilly, S; Lancet 1986, V2, P360 MEDLINE
(47) Piaditis, G; Clin Endocrinol 1996, V45, P595 HCAPLUS
(48) Pimenta, W; Diabet Med 1986, V13, PS33
(49) Pinto, G; Hormone Res 2000, V53, P163 HCAPLUS
(50) Poretsky, L; Endocr Rev 1999, V20, P535 HCAPLUS
(51) Postic, C; Biochem J 1993, V293, P119 HCAPLUS
(52) Prelevic, G; Hum Reprod 1995, V10, P28 MEDLINE
(53) Ramsay, T; Endocrinol Metab Clin North Am 1996, V25, P847 HCAPLUS
(54) Reaven, G; Diabetologia 1989, V32, P52 HCAPLUS
(55) Reaven, G; Physiol Rev 1995, V75(3), P473 MEDLINE
(56) Satoh, N; Endocrinology 1997, V138, P947 HCAPLUS
(57) Schwartz, M; Nature 2000, V404, P661 HCAPLUS
(58) Sigal, R; Diabetes 1997, V46, P1025 HCAPLUS
(59) The Diabetes Control And Complications Trial Research Group; N Engl J Med 2000, V342, P381
(60) Thorens, B; Diabetes 1990, V39, P712 HCAPLUS
(61) Uk Prospective Diabetes Study Ukpds Group; Lancet 1998, V352, P837
(62) van Hagen, P; Eur J Endocrinol 2000, V143s, P43
(63) Velasquez-Mieyer, P; 11th International Congress of Endocrinology 2000, PP1054

(64) Velasquez-Mieyer, P; Int J Obesity 2003, V27, P219 HCAPLUS
(65) Who; Obesity - Prevention and Managing the Global Epidemic 1998
(66) Who Study Group; Prevention of Diabetes Mellitus 1994
(67) Wilson, S; Growth Hormone IGF Res 2001, V11, PS53
(68) Yanovski, S; N Engl J Med 2002, V346, P591 HCAPLUS
(69) York, D; Endocrinol Metab Clin North Am 1996, V25, P781 HCAPLUS
(70) Zimmet, P; Diabetologia 1978, V15, P23 HCAPLUS

IT **108736-35-2, Lanreotide**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(somatostatin receptor ligands therapeutic potential in treatment of obesity and diabetes)

RN 108736-35-2 HCAPLUS

CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)



L51 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:907419 HCAPLUS
DN 138:185372
ED Entered STN: 29 Nov 2002
TI Serum leptin levels in acromegaly - a significant role for adipose tissue and fasting insulin/glucose ratio
AU Bolanowski, Marek; Milewicz, Andrzej; Bidzinska, Bozena; Jedrzejuk, Diana; Daroszewski, Jacek; Mikulski, Emil
CS Department of Endocrinology and Diabetology, Wroclaw Medical University, Pol.
SO Medical Science Monitor (2002), 8(10), CR685-CR689
CODEN: MSMOFR; ISSN: 1234-1010
PB International Scientific Literature, Inc.
DT Journal
LA English
CC 14-8 (Mammalian Pathological Biochemistry)
AB Leptin plays an important role in controlling satiety and maintaining energy balance. Acromegaly is characterized by decreased fat, which increases after the disease is cured. Our objective was to investigate serum leptin in acromegaly in terms of disease activity, body fat content, insulin and glucose levels, and selected anthropometric variables. We examined 40 patients with acromegaly and 20 sex- and age-matched controls for the levels of serum GH, IGF-I, leptin, glucose, and insulin, and for body composition by DEXA, BMI and WHR. In 10 cases the acute effect on serum

leptin of a somatostatin analog, **lanreotide**, was studied. We observed lower leptin in patients with active acromegaly than in cured patients and controls. Body fat was higher in cured than active patients. In the patients, the authors found significant correlations ($p<0.05$) between leptin and percent body fat ($r=0.77$), leptin and body fat mass ($r=0.74$), leptin and fasting insulin ($r=0.62$), leptin and fasting insulin/glucose ratio ($r=0.97$), leptin and BMI ($r=0.44$); leptin and height ($r=-0.47$). In the controls there was a significant correlation ($p<0.05$) only between leptin and WHR ($r=-0.45$). A paradoxical decrease of the leptin level after **lanreotide** was observed in 7 out of 10 patients with active acromegaly. Conclusions: Changes in leptin release in acromegaly are related to differences in body fat content and mass, and in insulin resistance. Leptin in acromegaly is not influenced directly by GH or IGF-I secretion. The acute effect of medical treatment of acromegaly by a somatostatin analog on leptin levels differs from the effect of a radical cure following pituitary adenoma surgery.

ST acromegaly blood leptin insulin glucose adipose tissue sex

IT **Obesity**
(obesity, serum leptin, adipose tissue, and fasting insulin/glucose ratio in acromegaly)

IT Acromegaly
Adipose tissue
Human
(serum leptin, adipose tissue, and fasting insulin/glucose ratio in acromegaly)

IT Sex
(sex differences in serum leptin, adipose tissue, and fasting insulin/glucose ratio in acromegaly)

IT 50-99-7, D-Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood; serum leptin, adipose tissue, and fasting insulin/glucose ratio in acromegaly)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(serum leptin, adipose tissue, and fasting insulin/glucose ratio in acromegaly)

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Bengtsson, B; Clin Endocrinol 1989, V30, P121 MEDLINE
(2) Berneis, K; Eur J Endocrinol 1996, V135, P663 HCAPLUS
(3) Bolanowski, M; Pituitary adenomas: From basic research to diagnosis and therapy 1996, P69 HCAPLUS
(4) Campfield, L; Horm Metab Res 1996, V28, P619 HCAPLUS
(5) Collins, S; Nature 1996, V380, P677 HCAPLUS
(6) Damjanovic, S; J Clin Endocrinol Metab 2000, V85, P147 HCAPLUS
(7) Davidson, M; Endocr Rev 1987, V8, P115 HCAPLUS
(8) DeFronzo, R; Am J Physiol 1979, V273, PE214
(9) Donahoo, W; J Clin Endocrinol Metab 1997, V82, P4139 HCAPLUS
(10) Florkowski, C; Clin Endocrinol 1996, V45, P769 HCAPLUS
(11) Gill, M; J Clin Endocrinol Metab 1999, V84, P1288 HCAPLUS
(12) Havel, P; J Clin Endocrinol Metab 1996, V81, P4406 HCAPLUS
(13) Ho, K; Clin Endocrinol 1992, V36, P271 MEDLINE
(14) Isidori, A; J Clin Endocrinol Metab 2000, V85, P1954 HCAPLUS
(15) Karlsson, C; Eur J Endocrinol 1998, V128, P408
(16) Katz, A; J Clin Endocrinol Metab 2000, V85, P2402 HCAPLUS
(17) Larsson, H; J Clin Endocrinol Metab 1998, V83, P4382 HCAPLUS
(18) Licinio, J; J Clin Endocrinol Metab 1998, V83, P4140 HCAPLUS
(19) Lonnqvist, F; Int J Obesity 1997, V21, P255 MEDLINE
(20) Matthews, D; Diabetologia 1985, V28, P412 HCAPLUS
(21) Miyakawa, M; J Clin Endocrinol Metab 1998, V83, P3476 HCAPLUS
(22) Salbe, A; J Clin Invest 1997, V99, P592 HCAPLUS
(23) Salomon, F; N Engl J Med 1989, V321, P1797 MEDLINE
(24) Schwartz, M; J Clin Invest 1996, V98, P1101 HCAPLUS

(25) Tan, K; Clin Endocrinol 2001, V54, P31 HCAPLUS

L51 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:814832 HCAPLUS
DN 137:333526
ED Entered STN: 25 Oct 2002
TI Method of treating obesity in adult patients exhibiting primary insulin hypersecretion by administering somatostatin
IN Lustig, Robert H.
PA USA
SO U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K038-31
NCL 514012000
CC 2-5 (Mammalian Hormones)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002156010	A1	20021024	US 2001-6738	20011108
PRAI US 2000-252324P	P	20001120		

AB Methods of treating obesity in adult patients, reducing the caloric intake in an obese adult patient, and inhibiting insulin hypersecretion in an obese adult patient are disclosed. The methods are practiced by administering to an obese adult patient exhibiting primary insulin hypersecretion an effective amount of somatostatin, a somatostatin receptor agonist or its salt, or combinations thereof, under conditions effective to reduce the weight of the obese adult patient, reduce the caloric intake of the obese adult patient, or inhibit insulin hypersecretion by pancreatic β-cells of the obese adult patient. Adults exhibiting primary insulin hypersecretion were treated with six injections of octreotide-LAR.
ST somatostatin treatment obesity; insulin hypersecretion inhibition somatostatin obesity; octreotide LAR wt loss
IT Somatostatin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SSTR2, agonists; method of treating obesity in adult patients exhibiting primary insulin hypersecretion by administering somatostatin)
IT Somatostatin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SSTR5, agonists; method of treating obesity in adult patients exhibiting primary insulin hypersecretion by administering somatostatin)
IT Somatostatin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; method of treating obesity in adult patients exhibiting primary insulin hypersecretion by administering somatostatin)
IT Drug delivery systems
(injections, i.m.; method of treating obesity in adult patients exhibiting primary insulin hypersecretion by administering somatostatin)
IT Drug delivery systems
(injections, s.c.; method of treating obesity in adult patients exhibiting primary insulin hypersecretion by administering somatostatin)
IT **Antiobesity agents**
Calorific value
Human
Human groups
(method of treating obesity in adult patients exhibiting primary insulin hypersecretion by administering somatostatin)
IT Pancreatic islet of Langerhans

(β-cell; method of treating obesity in adult patients exhibiting primary insulin hypersecretion by administering somatostatin)

IT 9004-10-8, Insulin, biological studies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(hypersecretion; method of treating obesity in adult patients exhibiting primary insulin hypersecretion by administering somatostatin)

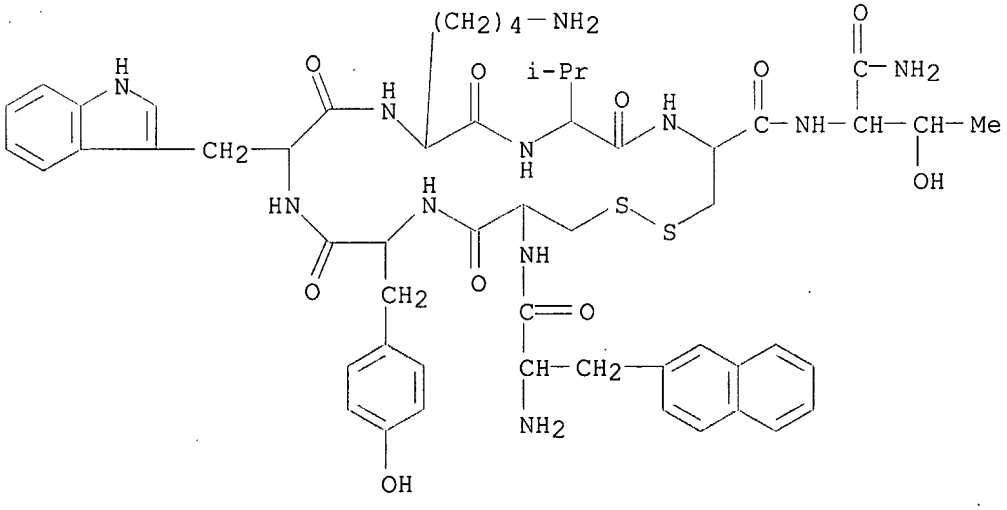
IT 51110-01-1, Somatostatin 51110-01-1D, Somatostatin, analogs 79517-01-4 83150-76-9, Octreotide **108736-35-2, Lanreotide**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of treating obesity in adult patients exhibiting primary insulin hypersecretion by administering somatostatin)

IT 38916-34-6, Somatostatin (sheep)
RL: PRP (Properties)
(unclaimed protein sequence; method of treating obesity in adult patients exhibiting primary insulin hypersecretion by administering somatostatin)

IT 473908-99-5
RL: PRP (Properties)
(unclaimed sequence; method of treating obesity in adult patients exhibiting primary insulin hypersecretion by administering somatostatin)

IT **108736-35-2, Lanreotide**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of treating obesity in adult patients exhibiting primary insulin hypersecretion by administering somatostatin)

RN 108736-35-2 HCAPLUS
CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)



L51 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:793646 HCAPLUS
DN 137:295256
ED Entered STN: 18 Oct 2002
TI Preparation of cyclic peptides as somatostatin agonists
IN Coy, David H.; Rajeswaran, Walajapet G.
PA The Administrators of the Tulane Educational Fund, USA

SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 2
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002081499	A2	20021017	WO 2002-US10882	20020408
WO 2002081499	A3	20030508		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-282526P P 20010409
OS MARPAT 137:295256
AB The invention is directed to cyclic peptides A1-cyclo[Cys-A2-D-Trp-A3-A4-Cys]-A5-Y1 [A1 is an optionally-substituted D- or L-aromatic α-amino acid or D- or L-cyclo(C3-6)alkylalanine; A2 is an optionally-substituted aromatic α-amino acid or cyclo(C3-6)alkylalanine; A3 is Lys or Orn; A4, A5 = β-hydroxyvaline, Ser, hSer, or Thr; Y1 is OH, NH2 or alkylamino; the substituent on the aromatic .vsigma.-amino acid or cyclo(C3-6)alkylalanine is selected from halogen, NO2, OH, CN, alkyl, alkenyl, alkynyl, alkoxy, Bzl, O-Bzl, or an amino group; the amine nitrogen of each amide peptide bond and the amino group of A1 is optionally substituted with a Me group (there is at least one Me group)] and their pharmaceutically-acceptable salts for use as somatostatin agonists. The solid-phase method was applied to the synthesis of 18 cyclic peptides of the invention, including NMe-D-Phe-cyclo[Cys-Phe-D-Trp-Lys-Thr-Cys]-Thr-NH2 (1). Peptide 1 showed binding affinities Kd for cloned human sst1-5 receptors of 316 ± 11, 1.03 ± 0.26, 17.9 ± 2.5, >1.000, and 4.89 ± 1.4 nM, resp., and agonist activity IC50 = 0.32 ± 0.13 nM on culture rat pituitary cells.
ST cyclic peptide prepn somatostatin agonist
IT Intestine, disease
(Crohn's; preparation of cyclic peptides as somatostatin agonists)
IT Bone, disease
(Paget's; preparation of cyclic peptides as somatostatin agonists)
IT Pancreas, neoplasm
(Zollinger-Ellison syndrome; preparation of cyclic peptides as somatostatin agonists)
IT Cachexia
(cancerous; preparation of cyclic peptides as somatostatin agonists)
IT Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclic; preparation of cyclic peptides as somatostatin agonists)
IT **Body weight**
(decreasing; preparation of cyclic peptides as somatostatin agonists)
IT Neoplasm
(gastrinoma; preparation of cyclic peptides as somatostatin agonists)
IT Digestive tract, disease
(gastroesophageal reflux; preparation of cyclic peptides as somatostatin agonists)

IT Gonadotropins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gonadotropinoma; preparation of cyclic peptides as somatostatin agonists)
IT Digestive tract, disease
(hemorrhage, upper; preparation of cyclic peptides as somatostatin agonists)
IT Liver, neoplasm
(hepatoma; preparation of cyclic peptides as somatostatin agonists)
IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia; preparation of cyclic peptides as somatostatin agonists)
IT Diarrhea
(hypersecretory diarrhea; preparation of cyclic peptides as somatostatin agonists)
IT Intestine, disease
(irritable bowel syndrome; preparation of cyclic peptides as somatostatin agonists)
IT Meninges
(neoplasm, meningioma; preparation of cyclic peptides as somatostatin agonists)
IT Pancreas, disease
(pancreatitis; preparation of cyclic peptides as somatostatin agonists)
IT Anxiety
(panic disorder; preparation of cyclic peptides as somatostatin agonists)
IT Solid phase synthesis
(peptide; preparation of cyclic peptides as somatostatin agonists)
IT Ovary, disease
(polycystic; preparation of cyclic peptides as somatostatin agonists)
IT AIDS (disease)
Acromegaly
Antihypotensives
Antitumor agents
Cushing's syndrome
Fibrosis
Graves' disease
Human
Hyperparathyroidism
Hypotension
Leukemia
Lung, neoplasm
Melanoma
Neoplasm
Psoriasis
Thyroid gland, neoplasm
(preparation of cyclic peptides as somatostatin agonists)
IT Somatostatin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of cyclic peptides as somatostatin agonists)
IT Pituitary gland, anterior lobe, neoplasm
(prolactinoma; preparation of cyclic peptides as somatostatin agonists)
IT Artery, disease
(restenosis; preparation of cyclic peptides as somatostatin agonists)
IT Connective tissue, disease
(scleroderma; preparation of cyclic peptides as somatostatin agonists)
IT Intestine
(small, obstruction; preparation of cyclic peptides as somatostatin agonists)
IT Disease, animal
(syndrome X; preparation of cyclic peptides as somatostatin agonists)
IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperinsulinism; preparation of cyclic peptides as somatostatin agonists)
IT 9002-62-4, Prolactin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)

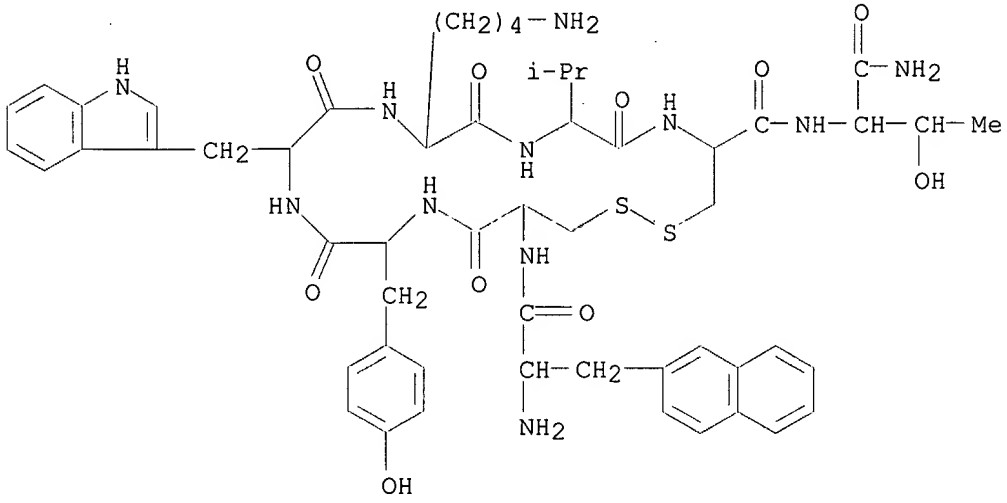
(hyperprolactinemia; preparation of cyclic peptides as somatostatin agonists)

IT 51110-01-1, Somatostatin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of cyclic peptides as somatostatin agonists)

IT 72127-57-2DP, N-Me derivs. 72127-59-4DP, N-Me derivs. 72127-61-8DP, N-Me derivs. 72127-62-9DP, N-Me derivs. 76080-70-1DP, N-Me derivs. 76587-47-8DP, N-Me derivs. 76587-65-0DP, N-Me derivs. 76587-78-5DP, N-Me derivs. 77236-35-2DP, N-Me derivs. 77236-36-3DP, N-Me derivs. 77236-39-6DP, N-Me derivs. 77236-42-1DP, N-Me derivs. 77236-46-5DP, N-Me derivs. 77286-22-7DP, N-Me derivs. 77286-23-8DP, N-Me derivs. 79775-25-0DP, N-Me derivs. 79775-28-3DP, N-Me derivs. 79814-97-4DP, N-Me derivs. 81377-02-8DP, N-Me derivs. 83150-76-9DP, N-Me derivs. 85003-75-4DP, N-Me derivs. 85466-72-4DP, N-Me derivs. 85466-73-5DP, N-Me derivs. 85466-74-6DP, N-Me derivs. 85549-65-1DP, N-Me derivs. 87778-83-4DP, N-Me derivs. 87781-70-2DP, N-Me derivs. 90836-21-8DP, N-Me derivs. 95310-74-0DP, N-Me derivs. 98044-71-4DP, N-Me derivs. 99660-13-6DP, N-Me derivs. 99685-66-2DP, N-Me derivs. 99685-66-2P 103140-93-8DP, N-Me derivs. 103222-11-3DP, N-Me derivs. 103335-28-0DP, N-Me derivs. 103335-29-1DP, N-Me derivs. 103429-37-4DP, N-Me derivs. 105407-44-1DP, N-Me derivs. **108736-35-2DP**, N-Me derivs. 109605-18-7DP, N-Me derivs. 109790-92-3DP, N-Me derivs. 109790-93-4DP, N-Me derivs. 109985-46-8DP, N-Me derivs. 111857-96-6DP, N-Me derivs. 116861-48-4DP, N-Me derivs. 117580-23-1DP, N-Me derivs. 117580-24-2DP, N-Me derivs. 117603-43-7DP, N-Me derivs. 120796-12-5DP, N-Me derivs. 123619-62-5DP, N-Me derivs. 129357-01-3DP, N-Me derivs. 129357-02-4DP, N-Me derivs. 129357-03-5DP, N-Me derivs. 129357-04-6DP, N-Me derivs. 129357-05-7DP, N-Me derivs. 129357-06-8DP, N-Me derivs. 129357-07-9DP, N-Me derivs. 129357-08-0DP, N-Me derivs. 129357-09-1DP, N-Me derivs. 129357-10-4DP, N-Me derivs. 129357-11-5DP, N-Me derivs. 129357-12-6DP, N-Me derivs. 129357-14-8DP, N-Me derivs. 129357-15-9DP, N-Me derivs. 129357-16-0DP, N-Me derivs. 129357-17-1DP, N-Me derivs. 129357-18-2P 129385-19-9DP, N-Me derivs. 129385-20-2DP, N-Me derivs. 129385-21-3DP, N-Me derivs. 129385-22-4DP, N-Me derivs. 133073-82-2DP, N-Me derivs. 133073-83-3DP, N-Me derivs. 133073-84-4DP, N-Me derivs. 133073-85-5DP, N-Me derivs. 138248-88-1DP, N-Me derivs. 138248-89-2DP, N-Me derivs. 144776-53-4DP, N-Me derivs. 147159-51-1DP, N-Me derivs. 150155-54-7DP, N-Me derivs. 150155-55-8DP, N-Me derivs. 150155-57-0DP, N-Me derivs. 150155-64-9DP, N-Me derivs. 150155-66-1DP, N-Me derivs. 163687-44-3DP, N-Me derivs. 181650-80-6DP, N-Me derivs. 184841-24-5DP, N-Me derivs. 204387-96-2DP, N-Me derivs. 204388-02-3DP, N-Me derivs. 204388-03-4DP, N-Me derivs. 204388-05-6DP, N-Me derivs. 204388-06-7DP, N-Me derivs. 204388-08-9DP, N-Me derivs. 204388-09-0DP, N-Me derivs. 204388-10-3DP, N-Me derivs. 204388-11-4DP, N-Me derivs. 215937-92-1DP, N-Me derivs. 215945-52-1DP, N-Me derivs. 216259-56-2DP, N-Me derivs. 216259-57-3DP, N-Me derivs. 216259-58-4DP, N-Me derivs. 216259-59-5DP, N-Me derivs. 216259-60-8DP, N-Me derivs. 216259-62-0DP, N-Me derivs. 216259-63-1DP, N-Me derivs. 216259-64-2DP, N-Me derivs. 216259-65-3DP, N-Me derivs. 216259-66-4DP, N-Me derivs. 216259-67-5DP, N-Me derivs. 216300-25-3DP, N-Me derivs. 247032-68-4DP, N-Me derivs. 247032-69-5DP, N-Me derivs. 340821-10-5P 340821-11-6P 340821-12-7P 340821-13-8P 340821-14-9P 340821-15-0P 340821-16-1P 340821-17-2P 340821-18-3P 340821-19-4P 340821-20-7P 340821-21-8P 340821-22-9P 340821-23-0P 340821-24-1P 340821-25-2P 340821-26-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclic peptides as somatostatin agonists)

IT **108736-35-2DP**, N-Me derivs.
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclic peptides as somatostatin agonists)

RN 108736-35-2 HCAPLUS
CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)



L51 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:276518 HCAPLUS
DN 136:304089
ED Entered STN: 12 Apr 2002
TI Method of treating insulin insensitivity and syndrome X
IN **Cawthorne, Michael Anthony; Liu, Yong-ling; Sennitt, Matthew V.**
PA UK
SO U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K038-00
ICS C07K005-00; C07K007-00; C07K016-00; C07K017-00; A61K038-12
NCL 514015000
CC 1-10 (Pharmacology)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002042374	A1	20020411	US 1998-76948	19980513 <--
PRAI US 1997-46373P	P	19970513 <--		

OS MARPAT 136:304089
AB The present invention relates to a method of treating insulin resistance or syndrome X in a patient. The method includes the step of administering a therapeutically effective amount of a somatostatin or a somatostatin agonist to said patient. Among examples provided are: binding of several somatostatin agonists to human somatostatin receptors, improvement of insulin sensitivity in BIM-23268-treated fatty Zucker rats, and reduction of hypertriglyceridemia by BIM-23268C in **obese** Zucker rats.
ST somatostatin agonist insulin resistance treatment
IT Somatostatin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SSTR1; somatostatin and somatostatin agonists in treatment of insulin insensitivity and syndrome X)
IT Somatostatin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(SSTR2; somatostatin and somatostatin agonists in treatment of insulin insensitivity and syndrome X)

IT Somatostatin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SSTR3; somatostatin and somatostatin agonists in treatment of insulin insensitivity and syndrome X)

IT Somatostatin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SSTR4; somatostatin and somatostatin agonists in treatment of insulin insensitivity and syndrome X)

IT Somatostatin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SSTR5; somatostatin and somatostatin agonists in treatment of insulin insensitivity and syndrome X)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia; somatostatin and somatostatin agonists in treatment of insulin insensitivity and syndrome X)

IT **Body weight**
(**loss**; somatostatin and somatostatin agonists in treatment of insulin insensitivity and syndrome X)

IT Hypertriglyceridemia
Obesity
(somatostatin and somatostatin agonists in treatment of insulin insensitivity and syndrome X)

IT Glycerides, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(somatostatin and somatostatin agonists in treatment of insulin insensitivity and syndrome X)

IT Disease, animal
(syndrome X; somatostatin and somatostatin agonists in treatment of insulin insensitivity and syndrome X)

IT 56-81-5, Glycerol, biological studies 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(somatostatin and somatostatin agonists in treatment of insulin insensitivity and syndrome X)

IT 51110-01-1, Somatostatin-14 75037-27-3, Somatostatin-28 83150-76-9, Octreotide **108736-35-2, BIM 23014**
133073-82-2, BIM 23052 168016-90-8, BIM 23197 181650-80-6, BIM 23268
182153-96-4, BIM 23190 189192-34-5, BIM 23284 189192-36-7, BIM 23295
215945-52-1, BIM 23272 216259-69-7, BIM 23313 412004-11-6, BIM 23268C
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(somatostatin and somatostatin agonists in treatment of insulin insensitivity and syndrome X)

IT 72127-57-2 72127-59-4 72127-61-8 72127-62-9 76080-70-1
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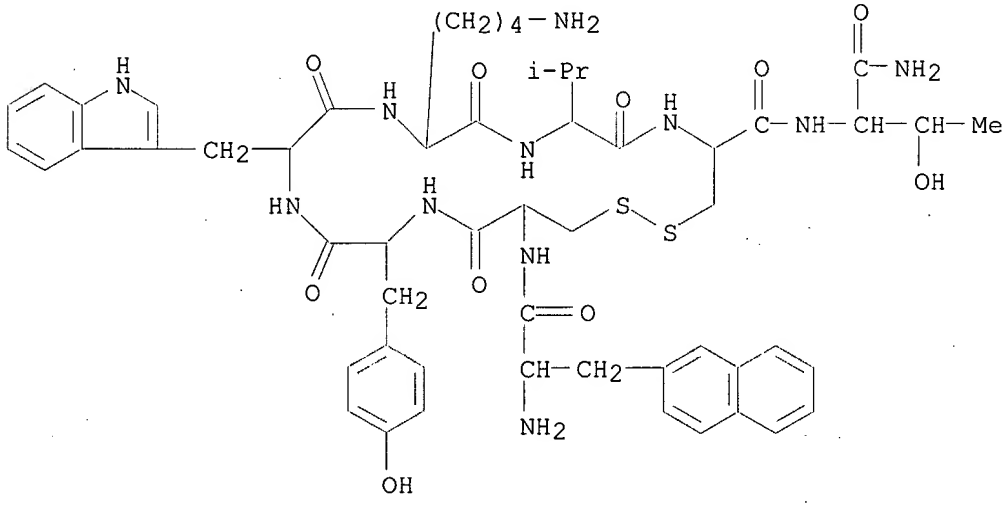
216259-66-4 216259-67-5 216300-25-3 247032-68-4 247032-69-5
410069-18-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(somatostatin and somatostatin agonists in treatment of insulin insensitivity and syndrome X)

IT **108736-35-2, BIM 23014**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(somatostatin and somatostatin agonists in treatment of insulin insensitivity and syndrome X)

RN 108736-35-2 HCAPLUS
CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)



L51 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:935632 HCAPLUS
DN 136:64088
ED Entered STN: 28 Dec 2001
TI A recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists
IN Lannoy, Vincent; Brezillon, Stephane; Detheux, Michel; Parmentier, Marc; Govarts, Cedric
PA Euroscreen S.A., Belg.
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K014-00
CC 1-1 (Pharmacology)
Section cross-reference(s): 9
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001098330	A2	20011227	WO 2001-BE104	20010620
WO 2001098330	A3	20020502		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1297003 A2 20030402 EP 2001-942923 20010620
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2004500125 T2 20040108 JP 2002-504285 20010620
PRAI US 2000-212913P P 20000620
US 2000-217494P P 20000711
EP 2001-870015 A 20010126
EP 2001-870024 A 20010212
WO 2001-BE104 W 20010620

AB The present invention is related to a G-protein coupled receptor or GPCRx11 similar to rat RTA receptor (37) and expressed in testis, thymus and uterus. Aequorin cell line expressing GPCRx11 has been used for screening of tissue exts. and reference ligands. GPCRx11 cells gave a specific signal with synthetic **angiopeptin** and a somatostatin analog allowing to validate this cell line for screening of natural or synthetic agonists and antagonists. In parallel, extended tissue distribution and polyclonal antibodies have been produced to facilitate GPCRx11 characterization.

ST recombinant cell line G protein receptor sequence screening

IT Antibodies
RL: BPN (Biosynthetic preparation); DGN (Diagnostic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(GPCRx11-specific; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Brain, disease
(Gilles de la Tourette syndrome; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Nervous system, disease
(Huntington's chorea; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Diagnosis
(agents; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Heart, disease
(angina pectoris; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Transgene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(animal expressing; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Antiarteriosclerotics
(antiatherosclerotics; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Infection
(bacterial; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Prostate gland, disease

(benign hyperplasia; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Mental disorder
(bipolar disorder; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT **Appetite**
(**bulimia**; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Drug delivery systems
(carriers; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Artery, disease
(coronary, restenosis; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Nervous system, disease
(degeneration; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Disease, animal
(degenerative; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Mental disorder
(delirium; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Mental disorder
(dementia; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Immunity
(disorder; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Nervous system, disease
(dyskinesia; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Heart, disease
(failure; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Bone, disease
(healing of; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Chromosome
(human 16; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Chromosome
(human 2; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Chromosome
(human 4; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Chromosome
(human 5; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)
IT Heart, disease
(infarction; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)
IT Animal
(knockout; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)
IT Antitumor agents
Neoplasm
(metastasis; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)
IT Headache
(migraine; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)
IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)
IT Molecular cloning
(of GPCRx11 receptor; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)
IT Mental disorder
(psychosis; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)
IT Alzheimer's disease
Analgesics
Aneurysm
Anorexia
Anti-Alzheimer's agents
Anti-inflammatory agents
Antibacterial agents
Antidepressants
Antidiabetic agents
Antiemetics
Antihypertensives
Antihypotensives
Antimigraine agents
Antiobesity agents
Antiparkinsonian agents
Antipsychotics
Antitumor agents
Antiulcer agents
Antiviral agents
Anxiety
Anxiolytics
Atherosclerosis
Cardiovascular system, disease
Cell migration
Diabetes mellitus
Drug screening
Genetic engineering
Genetic vectors
Human

Hypertension
Hypotension
Inflammation
Ischemia
Mental retardation
Neoplasm
Obesity
Osteoporosis
Pain
Parkinson's disease
Protein sequences
Schizophrenia
Test kits
Transformation, genetic
Ulcer
Urinary tract, disease
Vomiting
Wound healing
Wound healing promoters
cDNA sequences
(recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT G protein-coupled receptors
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Cell proliferation
(smooth muscle; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Muscle
(smooth, proliferation; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Brain, disease
(stroke; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT Infection
(viral; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT 383439-06-3 383439-08-5 383439-10-9 383439-12-1 383439-14-3
383439-16-5 383439-18-7 383439-20-1 383439-22-3 383439-24-5
383439-26-7
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT 383439-05-2 383439-07-4 383439-09-6 383439-11-0 383439-13-2
383439-15-4 383439-17-6 383439-19-8 383439-21-2 383439-23-4
383439-25-6
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT **108736-35-2** 383421-89-4 383439-36-9 383439-37-0

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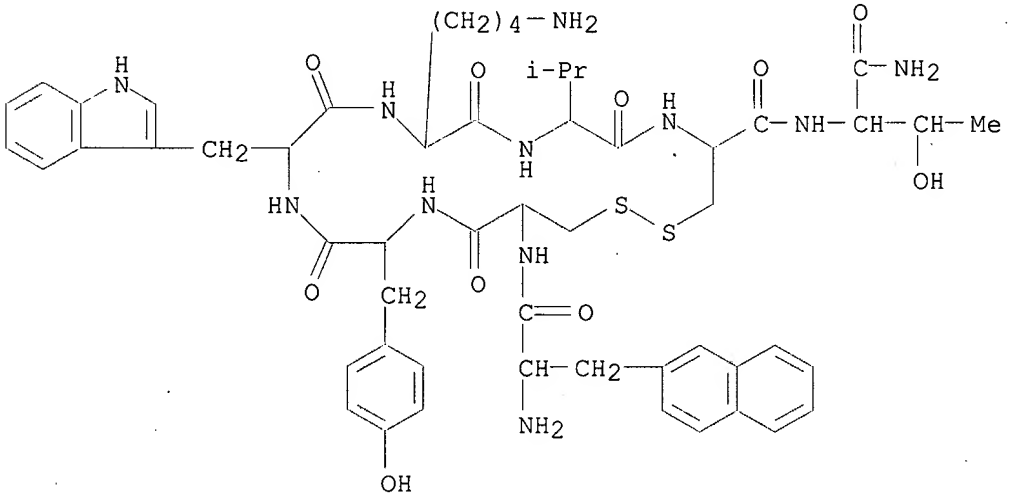
383439-43-8 383439-44-9 383439-45-0 383439-46-1 383439-47-2
383439-48-3 383439-49-4
RL: PRP (Properties)
(unclaimed sequence; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

IT **108736-35-2**
RL: PRP (Properties)
(unclaimed sequence; recombinant cell line expressing GPCRx11 as a functional receptor validated by **angiopeptin** and useful for screening of agonists and antagonists)

RN 108736-35-2 HCAPLUS
CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)



L51 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:764305 HCAPLUS
DN 130:20992
ED Entered STN: 07 Dec 1998
TI Somatostatin and somatostatin agonists for treating insulin insensitivity and Syndrome X
IN **Cawthorne, Michael Anthony; Liu, Yong-Ling; Sennitt, Matthew V.**
PA Societe De Conseils De Recherches Et D'Applications Scientifiques S.A. (S.C., Fr.
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-31
CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 63

Priority doc.

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9851332	A1	19981119	WO 1998-EP3000	19980513 <--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,

NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9880198 A1 19981208 AU 1998-80198 19980513 <--
EP 980253 A1 20000223 EP 1998-928308 19980513 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI

PRAI US 1997-854943 19970513 <--
WO 1998-EP3000 19980513

OS MARPAT 130:20992

AB The present invention relates to a method of treating insulin resistance or Syndrome X. The method includes the step of administering a therapeutically effective amount of a somatostatin or a somatostatin agonist to said patient. The invention also includes pharmaceutical compns. comprising a somatostatin or somatostatin agonist and the use of such products in the preparation of such compns.

ST somatostatin agonist insulin insensitivity Syndrome X treatment

IT Somatostatin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(SSTR2; somatostatin and somatostatin agonists for treating insulin insensitivity and Syndrome X)

IT Somatostatin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(SSTR5; somatostatin and somatostatin agonists for treating insulin insensitivity and Syndrome X)

IT Drug delivery systems
(pharmaceutical compns. containing somatostatin or somatostatin agonists for treating insulin insensitivity and Syndrome X)

IT Disease, animal
(syndrome X; somatostatin and somatostatin agonists for treating insulin insensitivity and Syndrome X)

IT 9004-10-8, Insulin, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(resistance; somatostatin and somatostatin agonists for treating insulin insensitivity and Syndrome X)

IT 51110-01-1, Somatostatin 72127-57-2 72127-59-4 72127-61-8
72127-62-9 76080-70-1 76587-47-8 76587-65-0 76587-78-5
77236-35-2 77236-36-3 77236-39-6 77236-42-1 77236-46-5
77286-22-7 77286-23-8 79775-25-0 79775-28-3 79814-97-4
81377-02-8 85466-72-4 85466-73-5 85466-74-6 85549-65-1
87778-83-4 87781-70-2 90836-21-8 95189-74-5 95310-74-0
98044-71-4 98044-76-9 99660-13-6 99685-66-2 103140-93-8
103222-11-3 103335-28-0 103335-29-1 103429-37-4 105407-44-1
108736-35-2 109605-18-7 109790-92-3 109790-93-4
109985-46-8 111857-96-6 113294-84-1 116861-48-4 117580-23-1
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129357-18-2 129385-19-9 129385-20-2 129385-21-3 129385-22-4
133073-82-2 133073-83-3 133073-84-4 133073-85-5 138248-88-1
138248-89-2 144776-53-4 147159-51-1 150155-55-8 150155-57-0
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204388-11-4 204388-13-6 204388-14-7 215937-92-1 215945-52-1
216259-56-2 216259-57-3 216259-58-4 216259-59-5 216259-60-8
216259-61-9 216259-62-0 216259-63-1 216259-64-2 216259-65-3
216259-66-4 216259-67-5 216259-68-6D, substituted-tyrosine derivative

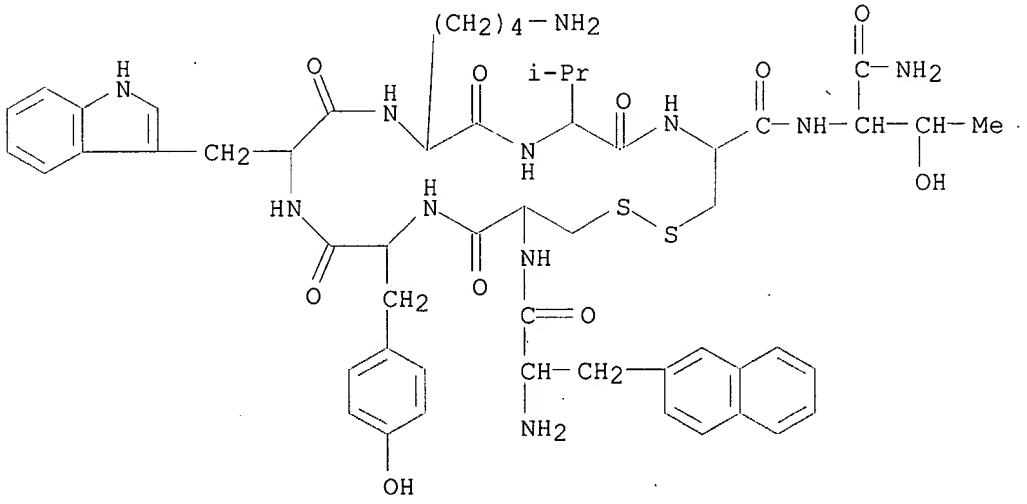
216259-69-7 216300-25-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(somatostatin and somatostatin agonists for treating insulin insensitivity and Syndrome X)

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE
(1) Biomeasure Inc; WO 9711962 A 1997 HCAPLUS
(2) Carretta, R; JOURNAL OF HYPERTENSION 1989, V7(SUPPL 06), PS196
(3) Cohen Yarom; WO 9810786 A 1998 HCAPLUS
(4) Davenport, M; DIABETOLOGIA 1995, V38(SUPPL 01), PA106
(5) Giustina, A; DIABETES RESEARCH AND CLINICAL PRACTICE 1991, V14, P47 MEDLINE
(6) Guillaume, G; REVUE MEDICALE DE BRUXELLES 1995, V16(2), P79 MEDLINE
(7) Kollind, M; ACTA ENDOCRINOLOGICA 1988, V118(2), P173 MEDLINE
(8) Mayo Foundation; EP 0657174 A 1995
(9) Sato, K; DATABASE BIOSIS HCAPLUS
(10) Sato, K; ENDOCRINE JOURNAL 1995, V42(6), P739 HCAPLUS
(11) Syntex Inc; EP 0363589 A 1990 HCAPLUS
(12) Univ Buckingham; WO 9635950 A 1996 HCAPLUS

IT **108736-35-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(somatostatin and somatostatin agonists for treating insulin insensitivity and Syndrome X)

RN 108736-35-2 HCAPLUS
CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)



L51 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:764304 HCAPLUS
DN 130:20991
ED Entered STN: 07 Dec 1998
TI Somatostatin and somatostatin agonists for decreasing **body weight**
IN **Cawthorne, Michael Anthony; Liu, Yong-Ling; Sennitt, Matthew V.**
PA Societe De Conseils De Recherches Et D'Applications Scientifiques S.A. (S.C., Fr.

SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-31
ICS A61K007-48
CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 62, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9851331	A1	19981119	WO 1998-EP2999	19980513 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9876550	A1	19981208	AU 1998-76550	19980513 <--
EP 981363	A1	20000301	EP 1998-924317	19980513 <--
EP 981363	B1	20030730		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 245998	E	20030815	AT 1998-924317	19980513 <--
PRAI US 1997-854941	A	19970513 <--		
WO 1998-EP2999	W	19980513 <--		

OS MARPAT 130:20991
AB The present invention relates to a method of decreasing **body weight** in a patient. The method includes the step of administering a therapeutically effective amount of a somatostatin or a somatostatin agonist to said patient. A pharmaceutical/cosmetic composition comprises the somatostatin or somatostatin agonist. Such products are used to prepare such compns. for the **reduction** of **body weight** in a human or mammalian animal.
ST somatostatin agonist **body wt redn**
IT Somatostatin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(SSTR2; somatostatin and somatostatin agonists for decreasing **body weight**)
IT Somatostatin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(SSTR5; somatostatin and somatostatin agonists for decreasing **body weight**)
IT Diabetes mellitus
(non-insulin-dependent; somatostatin and somatostatin agonists for decreasing **body weight** in patients with non-insulin dependent diabetes)
IT Cosmetics
Drug delivery systems
(pharmaceutical/cosmetic compns. containing somatostatin or somatostatin agonists for **weight reduction**)
IT **Antiobesity agents**
Body weight
(somatostatin and somatostatin agonists for decreasing **body weight**)
IT 51110-01-1, Somatostatin 72127-57-2 72127-59-4 72127-61-8
72127-62-9 76080-70-1 76587-47-8 76587-65-0 76587-78-5
77236-35-2 77236-36-3 77236-39-6 77236-42-1 77236-46-5
77286-22-7 77286-23-8 79775-25-0 79775-28-3 79814-97-4

81377-02-8 85466-72-4 85466-73-5 85466-74-6 85549-65-1
87778-83-4 87781-70-2 90836-21-8 95189-74-5 95310-74-0
98044-71-4 98044-76-9 99660-13-6 99685-66-2 103140-93-8
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108736-35-2 109605-18-7 109790-92-3 109790-93-4
109985-46-8 111857-96-6 113294-84-1 116861-48-4 117580-23-1
117580-24-2 117603-43-7 120796-12-5 123619-62-5 129357-01-3
129357-02-4 129357-03-5 129357-04-6 129357-05-7 129357-06-8
129357-07-9 129357-08-0 129357-09-1 129357-10-4 129357-11-5
129357-12-6 129357-14-8 129357-15-9 129357-16-0 129357-17-1
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150155-64-9 150155-66-1 163687-44-3 181650-80-6 184841-24-5
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216259-61-9 216259-62-0 216259-63-1 216259-64-2 216259-65-3
216259-66-4 216259-67-5 216259-68-6 216259-69-7 216300-25-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(somatostatin and somatostatin agonists for decreasing **body weight**)

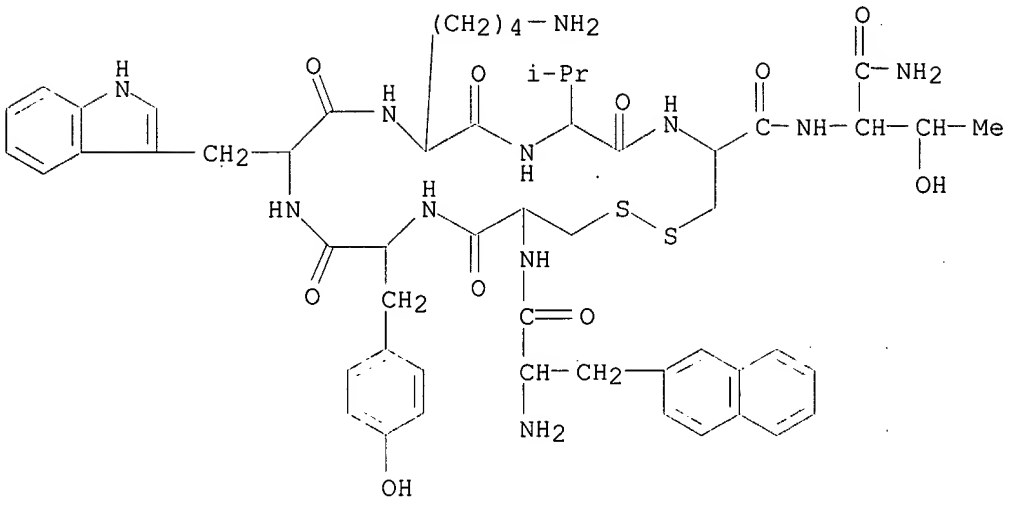
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Biomeasure Inc; WO 9711962 A 1997 HCAPLUS
(2) Carretta, R; JOURNAL OF HYPERTENSION 1989, V7(SUPPL 06), PS196
(3) Cohen Yarom; WO 9810786 A 1998 HCAPLUS
(4) Mayo Foundation; EP 0657174 A 1995
(5) Univ Buckingham; WO 9635950 A 1996 HCAPLUS
(6) Univ Washington; WO 9809991 A 1998 HCAPLUS

IT **108736-35-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(somatostatin and somatostatin agonists for decreasing **body weight**)

RN 108736-35-2 HCAPLUS
CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)



L51 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:244877 HCAPLUS
DN 129:776
ED Entered STN: 30 Apr 1998
TI Novel somatostatin analogs for the treatment of acromegaly and cancer exhibit improved in vivo stability and distribution
AU Gillespie, T. J.; Erenberg, A.; Kim, S.; Dong, J.; Taylor, J. E.; Hau, V.; Davis, T. P.
CS Department of Pharmacology, University of Arizona Health Sciences Center, Tucson, AZ, USA
SO Journal of Pharmacology and Experimental Therapeutics (1998), 285(1), 95-104
CODEN: JPETAB; ISSN: 0022-3565
PB Williams & Wilkins
DT Journal
LA English
CC 2-5 (Mammalian Hormones)
AB The bio-distribution of several radiolabeled somatostatin (SRIF) analogs was determined in the rat. Newly developed analogs BIM-23190 and BIM-23197 attained higher plasma levels and much greater target tissue concns. than the clin. used **BIM-23014** analog. Highest tissue concns. of BIM-23190 and BIM-23197 were found in adrenal, kidney, pituitary and pancreas, tissues that are known to be abundant in mRNA for the somatostatin subtype 2 receptor. BIM-23190 and BIM-23197 associated radioactivity in these tissues was prolonged compared with that of **BIM-23014**, especially in the SRIF-receptor-rich pituitary. BIM-23190 and BIM-23197 were more stable in vivo and much less subject to biliary excretion than **BIM-23014**. These properties account for the elevated plasma and target tissue concns. of these new SRIF analogs. Based on higher plasma levels, greater distribution to target tissues and longer in vivo stability, BIM-23190 and BIM-23197 may prove to be superior to **BIM-23014** for the treatment of acromegaly and some types of cancer.
ST somatostatin analog acromegaly cancer biodistribution stability
IT Acromegaly
Adipose tissue
Adrenal gland
Antitumor agents
Bile
Bladder
Blood plasma

Drug bioavailability
Drug metabolism
Epididymis
Eye
Heart
Intestine
Kidney
Liver
Lung
Muscle
Pancreas
Pancreatic islet of Langerhans
Pituitary gland
Skin
Stomach
Testis
Vas deferens
(somatostatin analogs for treatment of acromegaly and cancer exhibit improved in vivo stability and distribution)

IT 51110-01-1D, Somatostatin-14, analogs **108736-35-2, BIM -23014** 168016-90-8, BIM-23197 182153-96-4, BIM-23190
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(somatostatin analogs for treatment of acromegaly and cancer exhibit improved in vivo stability and distribution)

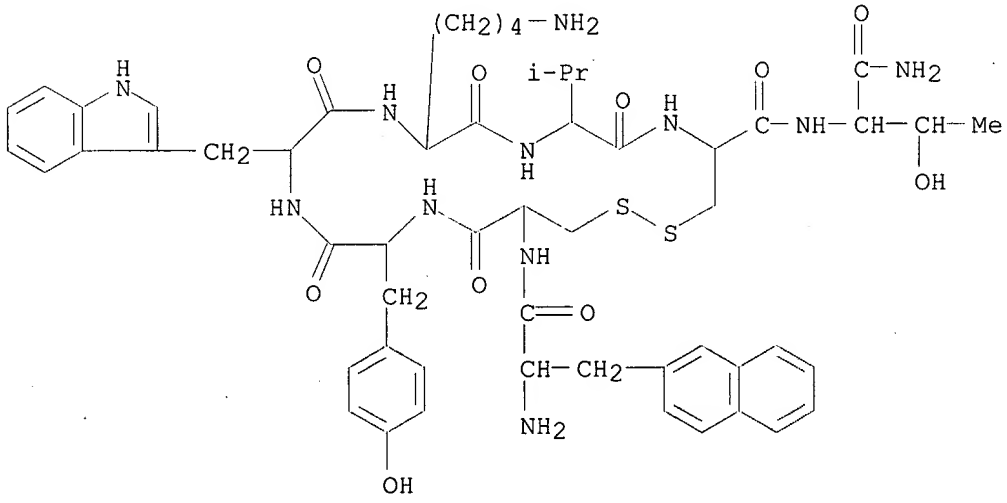
RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Abbruscato, T; J Pharmacol Exp Ther 1997, V280, P402 HCAPLUS
(2) Anthony, L; Acta Oncol 1993, V32, P217 MEDLINE
(3) Banks, W; Brain Res Bull 1994, V35, P179 HCAPLUS
(4) Bogden, A; Br J Cancer 1996, V73, P73 MEDLINE
(5) Bogden, A; Cancer Res 1990, V50, P2646 HCAPLUS
(6) Bogden, A; Cancer Res 1990, V50, P4360 HCAPLUS
(7) Brazeau, P; Science 1973, V179, P77 HCAPLUS
(8) Bruno, J; Endocrinology 1993, V133, P2561 HCAPLUS
(9) Bruns, C; Metabolism 1996, V45(suppl 1), P17
(10) Cai, R; Proc Natl Acad Sci USA 1986, V83, P1896 HCAPLUS
(11) Caron, P; Eur J Endocrinol 1995, V132, P320 HCAPLUS
(12) Coy, D; Metabolism 1996, V45(suppl 1), P21
(13) Epelbaum, J; J Clin Endocrinol Metab 1995, V80, P1837 HCAPLUS
(14) Epelbaum, J; J Neurochem 1982, V38, P1515 HCAPLUS
(15) Epelbaum, J; Prog Neurobiol 1986, V27, P63 HCAPLUS
(16) Evans, C; Science 1992, V258, P1952 HCAPLUS
(17) Gancel, A; Clin Endocrinol 1994, V40, P421 MEDLINE
(18) Gu, Z; Am J Physiol 1995, V268(5 pt 1), PG739 MEDLINE
(19) Heiman, M; Neuroendocrinology 1987, V45, P429 HCAPLUS
(20) Hoyer, D; Trends Pharmacol Sci 1995, V16, P86 HCAPLUS
(21) Kramer, T; J Pharmacol Exp Ther 1989, V249, P544 HCAPLUS
(22) Lemaire, M; Drug Metab Dispos 1989, V17, P699 HCAPLUS
(23) Liebow, C; Proc Natl Acad Sci USA 1989, V86, P2003 HCAPLUS
(24) Marek, J; Eur J Endocrinol 1994, V131, P20 MEDLINE
(25) Maulard, C; Cancer Chemother Pharmacol 1995, V36, P259 MEDLINE
(26) Morange, I; J Clin Endocrinol Metab 1994, V79, P145 MEDLINE
(27) Moreau, J; Life Sci 1987, V40, P419 HCAPLUS
(28) Moreau, J; Metabolism 1996, V45(suppl 1), P24
(29) O'Carroll, A; Mol Pharmacol 1994, V46, P291 HCAPLUS
(30) Patel, Y; Life Sci 1995, V57, P1249 HCAPLUS
(31) Patel, Y; Metabolism 1996, V45(suppl 1), P31
(32) Prevost, G; Life Sci 1994, V55, P155 HCAPLUS
(33) Raulf, F; Digestion 1994, V55(suppl 3), P46
(34) Reubi, J; Growth Factors, Peptides and Receptors 1993, P445 HCAPLUS
(35) Reubi, J; Life Sci 1981, V28, P2191 HCAPLUS

(36) Reubi, J; Metabolism 1990, V39(suppl 2), P78
(37) Reubi, J; Metabolism 1996, V45(suppl 1), P39
(38) Ruwart, M; Peptide-Based Drug Design:Controlling Transport and Metabolism, ed 1, ACS Professional Reference Book 1995, P251
(39) Scherubl, H; Eur J Cancer 1994, V30A, P1590 MEDLINE
(40) Schetz, J; J Pharmacol Exp Ther 1995, V274, P1456 HCAPLUS
(41) Setyono-Han, B; Cancer Res 1987, V47, P1566 HCAPLUS
(42) Srikant, C; Endocrinology 1985, V116, P1717 HCAPLUS
(43) Srikant, C; J Biol Chem 1986, V261, P7690 HCAPLUS
(44) Srikant, C; Proc Natl Acad Sci USA 1981, V78, P3920
(45) Tallarida, R; Manual of Pharmacologic Calculations with Computer Programs, ed 2 1987
(46) Tan, C; Gastroenterology 1995, V108, P1908 MEDLINE
(47) Taylor, J; Biochem Biophys Res Commun 1988, V153, P81 HCAPLUS
(48) Taylor, J; Growth Factors, Peptides and Receptors 1993, P181 HCAPLUS
(49) Thomas, F; Immunodeficient Mice in Oncology 1992
(50) Viollet, C; Fundam Clin Pharmacol 1995, V9, P107 HCAPLUS
(51) Wen, P; Curr Opin Oncol 1995, V7, P56 MEDLINE
(52) Woltering, E; Surgery 1994, V116, P1139 MEDLINE
(53) Yamada, Y; Proc Natl Acad Sci USA 1992, V89, P251 HCAPLUS
(54) Zeggari, M; Peptides 1986, V7, P953 HCAPLUS

IT **108736-35-2, BIM-23014**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(somatostatin analogs for treatment of acromegaly and cancer exhibit improved in vivo stability and distribution)

RN 108736-35-2 HCAPLUS

CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)



L51 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:9328 HCAPLUS
DN 126:27295
ED Entered STN: 09 Jan 1997
TI Inhibition of amylin release
IN Dunmore, Simon Jon; Davenport, Michelle; **Cawthorne, Michael Anthony**
PA University of Buckingham, UK
SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N033-50
ICS A61K038-31
CC 2-6 (Mammalian Hormones)
Section cross-reference(s): 1, 14
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9635950	A1	19961114	WO 1996-EP2064	19960511	<--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI					
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML					
	US 5763200	A	19980609	US 1995-440061	19950512	<--
	CA 2220106	AA	19961114	CA 1996-2220106	19960511	<--
	AU 9657645	A1	19961129	AU 1996-57645	19960511	<--
	AU 694360	B2	19980716			
	EP 829011	A1	19980318	EP 1996-914208	19960511	<--
	EP 829011	B1	20020828			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	JP 11505611	T2	19990521	JP 1996-533796	19960511	<--
	NZ 334487	A	20000728	NZ 1996-334487	19960511	<--
	AT 223045	E	20020915	AT 1996-914208	19960511	<--
	PT 829011	T	20030131	PT 1996-96914208	19960511	<--
	ES 2180769	T3	20030216	ES 1996-914208	19960511	<--
	US 2001006790	A1	20010705	US 1997-961968	19971031	<--
PRAI	US 1995-440061	A	19950512	<--		
	NZ 1996-308105	A1	19960511	<--		
	WO 1996-EP2064	W	19960511	<--		

AB A method is described for determining the ability of a compound to both bind to somatostatin type-5 receptor ("SSTR-5") and inhibit amylin release. The method includes obtaining a preparation, either a cell preparation or a membrane preparation, which contains SSTR-5; incubating the preparation, the compound, and an SSTR-5 ligand, at least one of the ligand and the compound being detectably labeled; determining the ability of the compound to compete against the ligand for binding to SSTR-5; if and only if the compound. is determined to be able to bind to SSTR-5, obtaining pancreatic cells; incubating the compound, the pancreatic cells, and an amylin release stimulator under conditions in which the amylin release stimulator would induce release of amylin from the pancreatic cells; and determining the ability of the compound to inhibit amylin release. Also disclosed is a method of treating hyperamylinemia with a ligand selective for SSTR-5.

ST somatostatin receptor binding compd identification; pancreas amylin release inhibitor identification; hyperamylinemia therapy SSTR5 peptide agonist

IT Animal cell line
(CHO-K1; identification of compds. binding to somatostatin type-5 receptor and inhibiting amylin release)

IT Animal cell line
(RINm5F; identification of compds. binding to somatostatin type-5 receptor and inhibiting amylin release)

IT Somatostatin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(SSTR5; identification of compds. binding to somatostatin type-5 receptor and inhibiting amylin release)

IT Biological transport
(efflux; identification of compds. binding to somatostatin type-5 receptor and inhibiting amylin release)

IT Membrane, biological
Pancreas
Pancreas, neoplasm
(identification of compds. binding to somatostatin type-5 receptor and inhibiting amylin release)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(identification of compds. binding to somatostatin type-5 receptor and inhibiting amylin release)

IT Diabetes mellitus
(non-insulin-dependent; identification of compds. binding to somatostatin type-5 receptor and inhibiting amylin release)

IT Brain
(olfactory bulb; identification of compds. binding to somatostatin type-5 receptor and inhibiting amylin release)

IT Diabetes mellitus
(pre-; identification of compds. binding to somatostatin type-5 receptor and inhibiting amylin release)

IT Pancreatic islet of Langerhans
(β-cell; identification of compds. binding to somatostatin type-5 receptor and inhibiting amylin release)

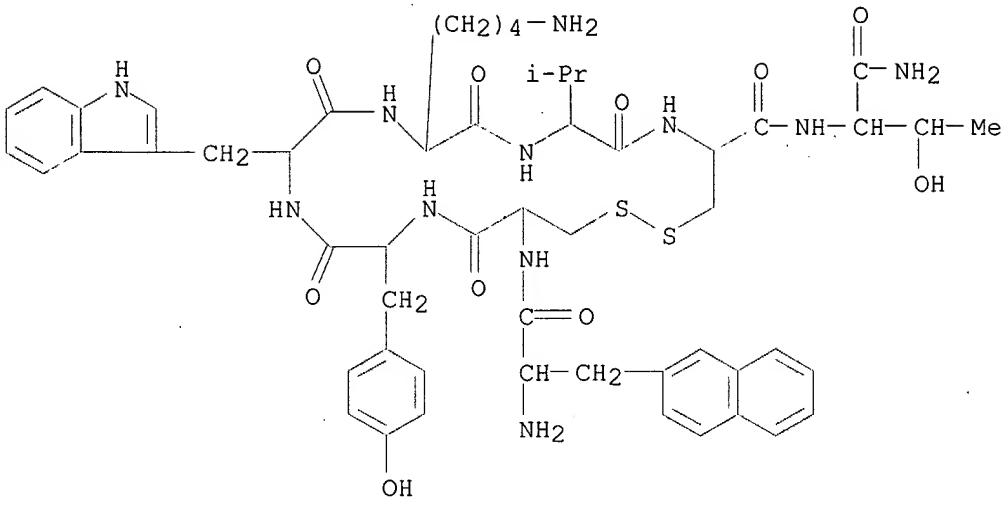
IT 51110-01-1, Somatostatin 83150-76-9, Sms 201-995 **108736-35-2, Lanreotide** 133073-82-2 133073-83-3 133073-84-4 150155-60-5 150155-64-9 150155-66-1 184841-23-4 184841-24-5 184841-25-6 184841-26-7
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(identification of compds. binding to somatostatin type-5 receptor and inhibiting amylin release)

IT 106602-62-4, Amylin
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(identification of compds. binding to somatostatin type-5 receptor and inhibiting amylin release)

IT **108736-35-2, Lanreotide**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(identification of compds. binding to somatostatin type-5 receptor and inhibiting amylin release)

RN 108736-35-2 HCAPLUS

CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)



L51 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1996:435653** HCAPLUS
DN **125:105481**
ED Entered STN: 24 Jul 1996
TI A dose-finding study of **lanreotide** (a somatostatin analog) in patients with colorectal carcinoma
AU Leo, Angelo Di; Bajetta, Emilio; Ferrari, Leonardo; Biganzoli, Laura; Mariani, Luigi; Carnaghi, Carlo; Camerini, Edgarda; Buzzoni, Roberto; Ruiz, Jean Marc
CS Division Medical Oncology B, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, 20133, Italy
SO Cancer (New York) (**1996**), 78(1), 35-42
CODEN: CANCAR; ISSN: 0008-543X
PB Wiley-Liss
DT Journal
LA English
CC 2-5 (Mammalian Hormones)
AB Laboratory data suggest that insulin-like growth factor-1 (IGF-1) may stimulate the growth of different human tumors. At least in acromegalic patients, somatostatin (SMS) analogs, such as **lanreotide**, suppress the serum levels of growth hormone (GH) and IGF-1. To evaluate the tolerability and biol. activity of different doses of **lanreotide** in patients with advanced colorectal carcinoma, consecutive groups of 3 patients each were s.c. treated with **lanreotide** at doses of 1, 2, 3, 4, 5, or 6 mg three times a day for 2 mo. In the event of Grade 3 side effects, 3 addnl. patients were treated with the same dose before the next dose escalation. Serum samples were obtained on Days 0, 15, 30, and 60 for serum GH, IGF-1, and **lanreotide** assessment. Twenty-four patients were enrolled and all were evaluable. Except for the 3 and 6 mg doses, for which the observation of a Grade 3 side effect required that an addnl. three patients be treated, it was sufficient to treat 3 patients at each dose. The overall incidence of side effects was as follows: changes in bowel habits, 83%; abdominal cramps, 79%; diarrhea, 17%; vomiting, 17%; nausea, 21%; steatorrhea, 78%; hyperglycemia, 35%; laboratory hypothyroidism, 39%; gallstones, 13%; and **weight loss**, 17%. No evidence of an increase in the incidence, intensity, or duration of side effects was observed with dose escalation. Serum IGF-1 levels were as follows: Day 15: 63%, 60%, and 67% of the baseline values for the low (1-2 mg), intermediate (3-4 mg), and high (5-6 mg) dose groups, resp.; Day 30: 63%, 59%, and 51%, resp.; and Day 60: 73%, 69%, and 47%, resp. Serum **lanreotide** levels declined during treatment in all of the dose

groups (90 ng/mL on Day 15, and 35 ng/mL on Day 60 for the 5-6 mg group; 10 ng/mL on Day 15, and 1.5 ng/mL on Day 60 for the 1-2 mg group). No antitumor activity or tumor marker **reduction** was observed No increase in toxicity was observed when s.c. **lanreotide** doses were escalated to 6 mg three times a day for 2 mo. The highest doses seemed to maintain **reduced** serum IGF-1 levels; with the lowest doses, a "rebound" in serum IGF-1 levels was observed during treatment. Nevertheless, intermittent s.c. injections do not ensure constant serum drug concns. over time.

ST **lanreotide** somatotropin IGF colorectal carcinoma

IT Intestine, neoplasm
(large, carcinoma, dose-finding study of **lanreotide** (a somatostatin analog) in human patients with colorectal carcinoma)

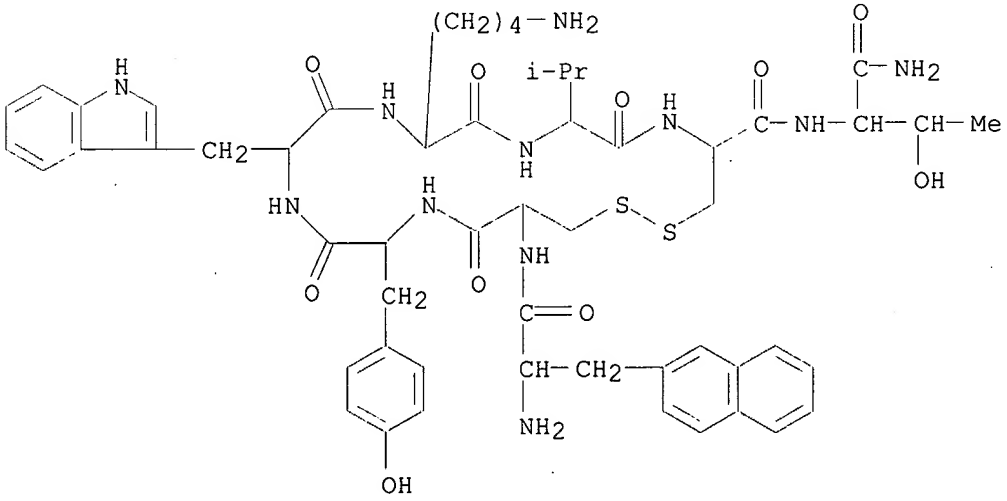
IT **108736-35-2, Lanreotide**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(dose-finding study of **lanreotide** (a somatostatin analog) in human patients with colorectal carcinoma)

IT 9002-72-6, Growth hormone 67763-96-6, IGF-1
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(dose-finding study of **lanreotide** (a somatostatin analog) in human patients with colorectal carcinoma)

IT **108736-35-2, Lanreotide**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(dose-finding study of **lanreotide** (a somatostatin analog) in human patients with colorectal carcinoma)

RN 108736-35-2 HCAPLUS

CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)



=> => fil medline
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FILE LAST UPDATED: 10 FEB 2004 (20040210/UP). FILE COVERS 1958 TO DATE.

On December 14, 2003, the 2004 MeSH terms were loaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http:\\www.nih.gov/pubs/yechbull/nd03/nd03_mesh.html for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all l78

L78 ANSWER 1 OF 1 MEDLINE on STN
AN 2003405563 MEDLINE
DN PubMed ID: 12943494
TI The therapeutic potential of somatostatin receptor ligands in the treatment of **obesity** and diabetes.
AU Boehm Bernhard O
CS Division of Endocrinology, University of Ulm, Germany.. bernhard.boehm@medizin.uni-ulm.de
SO Expert opinion on investigational drugs, (2003 Sep) 12 (9) 1501-9. Ref: 70
Journal code: 9434197. ISSN: 1354-3784.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200401
ED Entered STN: 20030829
Last Updated on STN: 20040107
Entered Medline: 20040106
AB Since the development of synthetic somatostatin analogues, several therapeutic applications for somatostatin receptor agonist molecules have been defined. Established applications for somatostatin analogue treatment include pituitary tumours (growth hormone and thyrotropin-secreting adenomas), neuroendocrine tumours of the pancreas and gastrointestinal tract (so-called carcinoid tumours, vasoactive intestinal tumours) and gastroenterological conditions (pancreatitis, gastrointestinal bleedings, refractory diarrhoeas, pancreatic and intestinal fistulas, diarrhoea in AIDS). Further areas for development of somatostatin analogue therapy include **obesity**, polycystic ovary syndrome and diabetes mellitus, dysmetabolic conditions that are often interrelated. The challenge for the future will be to transform results from clinical trials conducted in heterogeneous clinical situations into novel options of somatostatin analogue use. Since **obesity** and diabetes mellitus both are disorders of marked heterogeneity, the subgroup of patients that will benefit most from somatostatin analogue treatment has yet to be defined. In addition, the development of more universal ligands covering all of the known somatostatin receptor molecules as well as receptor subtype specific agents is currently underway. The establishment of slow-release depot formulations of octreotide and **lanreotide** has already provided a more acceptable and consistent delivery mechanism. Use of biodegradable polymer microsphere formulations provides the basis for the development of novel applications, which include hyperinsulinaemia, **obesity** and polycystic ovary syndrome as components of the dysmetabolic syndrome. The most developed thus far is the use of octreotide in hyperinsulinaemic forms of **obesity** and in distinct stages of diabetic retinopathy.
CT Check Tags: Female; Human; Support, Non-U.S. Gov't

*Diabetes Mellitus: DT, drug therapy
Diabetes Mellitus: ME, metabolism
Diabetic Retinopathy: DT, drug therapy
Diabetic Retinopathy: ME, metabolism
Ligands
Metabolic Syndrome X: DT, drug therapy
Metabolic Syndrome X: ME, metabolism
***Obesity: DT, drug therapy**
Obesity: ME, metabolism
Polycystic Ovary Syndrome: DT, drug therapy
Polycystic Ovary Syndrome: ME, metabolism
*Receptors, Somatostatin: ME, metabolism
Somatostatin: AA, analogs & derivatives
Somatostatin: PD, pharmacology
Somatostatin: TU, therapeutic use
RN 51110-01-1 (Somatostatin)
CN 0 (Ligands); 0 (Receptors, Somatostatin)

=> => fil biosis
FILE 'BIOSIS' ENTERED AT 08:20:03 ON 11 FEB 2004
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 4 February 2004 (20040204/ED)

FILE RELOADED: 19 October 2003.

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L88 ANSWER 1 OF 1 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1997:170348 BIOSIS
DN PREV199799476951
TI Can we substitute **lanreotide** for octreotide in the treatment of severe postgastrectomy dumping syndrome?.
AU Bouche, Olivier; Salmon-Ettersperger, Laurence; Fremond, Luc; Thiefin, Gerard; Zeitoun, Paul
CS Serv. Hepato-Gastroenterol., CHU Robert Debre, 51092 Reims Cedex, France
SO Gastroenterologie Clinique et Biologique, (1997) Vol. 21, No. 1, pp. 84-85.
CODEN: GCBIDC. ISSN: 0399-8320.
DT Letter
LA French
ED Entered STN: 24 Apr 1997
Last Updated on STN: 24 Apr 1997
CC Biochemistry studies - General 10060
Pathology - Therapy 12512
Digestive system - General and methods 14001
Pharmacology - General 22002
IT Major Concepts
Biochemistry and Molecular Biophysics; Digestive System (Ingestion and Assimilation); Pharmacology
IT Chemicals & Biochemicals
LANREOTIDE; OCTREOTIDE
IT Miscellaneous Descriptors
ADULT; **BODY WEIGHT**; CLINICAL EFFICACY; DAILY INJECTION ALTERNATIVE; DIGESTIVE SYSTEM DISEASE; DRUG DOSAGE; DUMPING SYNDROME; GASTROENTEROLOGY; GASTROINTESTINAL-DRUG; HORMONE-DRUG; **LANREOTIDE**; MALE; OCTREOTIDE; PATIENT; PHARMACOLOGY; POST-GASTRECTOMY COMPLICATION; PROLONGED RELEASE; QUALITY OF LIFE;

SYMPTOMATOLOGY
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN **108736-35-2 (LANREOTIDE)**
83150-76-9 (OCTREOTIDE)

=> => fil wpix
FILE 'WPIX' ENTERED AT 08:48:33 ON 11 FEB 2004
COPYRIGHT (C) 2004 THOMSON DERWENT

FILE LAST UPDATED: 10 FEB 2004 <20040210/UP>
MOST RECENT DERWENT UPDATE: 200410 <200410/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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available in the /ABEX field. An additional search field
/BIX is also provided which comprises both /BI and /ABEX <<<

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GUIDES, PLEASE VISIT:
http://thomsonderwent.com/support/userguides/ <<<

>>> ADDITIONAL POLYMER INDEXING CODES WILL BE IMPLEMENTED FROM
DERWENT UPDATE 200403.
THE TIME RANGE CODE WILL ALSO CHANGE FROM 018 TO 2004.
SDIS USING THE TIME RANGE CODE WILL NEED TO BE UPDATED.
FOR FURTHER DETAILS: http://thomsonderwent.com/chem/polymers/ <<<

=> d all abeq tech abex tot

L115 ANSWER 1 OF 15 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2004-099347 [10] WPIX
DNC C2004-041082
TI Growth hormone secretagogue receptor antagonist for treatment of diabetes, **obesity** and appetite control.
DC B04
IN ASAKAWA, A; INUI, A
PA (CHUS) CHUGAI SEIYAKU KK
CYC 105
PI WO 2004004772 A1 20040115 (200410)* JA 44p A61K045-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS
LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK

DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH
PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC
VN YU ZA ZM ZW
ADT WO 2004004772 A1 WO 2003-JP8482 20030703
PRAI JP 2002-197582 20020705
IC ICM A61K045-00
ICS A61K038-17; **A61P003-04**; A61P003-10; A61P043-00
AB WO2004004772 A UPAB: 20040210
NOVELTY - Treatment and preventative agent for diabetes comprises growth hormone secretagogue receptor (GHS-R) antagonist, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for a method for lowering blood sugar, treatment and prevention of **obesity**, an appetite controlling agent all using a GHS-R antagonist.
ACTIVITY - Antidiabetic; Anorectic.
MECHANISM OF ACTION - Growth hormone secretagogue receptor antagonist
USE - For treatment and prevention of diabetes, **obesity**, for lowering blood sugar levels and for use in controlling appetite (claimed).
Dwg.0/14
FS CPI
FA AB
MC CPI: **B04-J10**; B04-K01P; **B14-E12**; B14-S04
ABEX UPTX: 20040210
ADMINISTRATION - 0.1 micrograms-1000 mg/kg, preferably 0.1-10 mg/kg, i.v.

EXAMPLE - The effect of repeated administration of (D-Lys-3)-GHRP-6 on the weight gain and blood sugar level control in ob/ob mice was observed. The results, as shown in diagram 13, demonstrate that it reduces weight gain and blood sugar concentration without reducing muscle mass.

L115 ANSWER 2 OF 15 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2004-043123 [04] WPIX
DNC C2004-017852
TI Detecting specific glucose transport genes or proteins, useful for diagnosing a predisposition to **obesity**, comprises using a specific compound, such as an antibody.
DC B04 C06 D16
IN DIETER, M; LANG, F
PA (LANG-I) LANG F
CYC 103
PI WO 2003102206 A2 20031211 (200404)* DE 38p C12Q000-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
DE 10225844 A1 20031218 (200407) C12Q001-34
ADT WO 2003102206 A2 WO 2003-EP5847 20030604; DE 10225844 A1 DE 2002-10225844 20020604
PRAI DE 2002-10225844 20020604
IC ICM C12Q000-00; C12Q001-34
ICS A61K038-19; A61K038-55
AB WO2003102206 A UPAB: 20040115
NOVELTY - Use of at least one compound (I) for detecting expression and/or function of activated and/or inactivated proteins for diagnosis of diseases associated with disturbed glucose transport.
DETAILED DESCRIPTION - Use of at least one compound (I) for detecting expression and/or function of activated and/or inactivated Sgk (serum and glucocorticoid-dependent kinase), especially Sgk1 and/or 3; and/or PKB (protein kinase B) and/or Nedd (neural precursor cell expressed,

developmentally downregulated gene), especially Nedd4-2, for diagnosis of diseases associated with disturbed glucose transport.

INDEPENDENT CLAIMS are also included for the following:

(1) method for diagnosing a predisposition to **obesity** by detecting a polymorphism in the sgk, nedd, sglt (sodium-glucose transporter), especially sglt1, or PKB genes;

(2) use of at least one active agent (Ia) for modifying glucose transport, especially in intestines and kidneys;

(3) use of at least one active agent (Ib) for modifying, especially inhibiting, at least one Sglt and/or PKB, and/or for modulating, especially stimulating, at least one Nedd, for treatment of disorders associated with disturbed glucose transport;

(4) diagnostic kit containing at least one (I);

(5) antibodies (Ab) directed against at least one kinase consensus sequence that is phosphorylated, non-phosphorylated or mutated;

(6) composition containing at least one (Ia); and

(7) method for generating non-human transgenic animals with increased deposition of lipid in adipose tissue by increasing the expression and/or function of Sglt, particularly Sglt1.

ACTIVITY - Anorectic; Antidiabetic; Hypotensive; Anabolic.

MECHANISM OF ACTION - Modulating expression and/or activity of proteins involved in glucose transport. Specifically Nedd4-2 is an inactivator of Sglt and its effect is prevented by Sgk and/or PKB. Xenopus oocytes were injected with mRNA for Sglt1 then treated with glucose (20 mM). The mean inward glucose current was 48.6 nA, compare 1.3 nA for cells not injected with the mRNA. When both Sglt1 and Nedd4-2 RNAs were injected, the inward current was reduced by 49.2%, and co-transfection with all three of Sglt1, Sgk1 and Nedd4-2 mRNAs resulted in a current 34.8% greater than with Sglt1 alone.

USE - (I) are used to diagnose metabolic syndrome, especially **obesity** but also diabetes and hypertension. Also, detecting polymorphisms in the genes that encode the specified proteins can be used to identify a predisposition to **obesity** and diseases caused by disturbed glucose transport can be treated or prevented using agents that modulate expression and/or activity of these proteins. Alternatively, the agents can be used to increase body weight, specifically in animals; also to prepare transgenic animals.

Dwg.0/5

FS CPI

FA AB; DCN

MC CPI: B04-E02B; B04-E02E; B04-E09; B04-G03; B04-H01; B04-H06; B04-H06F; B04-J01; B04-J03A; **B04-J10**; B04-L04; B04-P0100E; B11-C07A; B11-C08E; B12-K04A; B12-K04F; B14-D06; B14-E11; **B14-E12**; B14-F02B; B14-S04; C04-E02B; C04-E02E; C04-E09; C04-G03; C04-H01; C04-H06; C04-H06F; C04-J01; C04-J03A; **C04-J10**; C04-L04; C04-P0100E; C11-C07A; C11-C08E; C12-K04A1; C12-K04F; C14-D06; C14-E11; **C14-E12**; C14-F02B; C14-S04; D05-H09; D05-H11; D05-H16A

TECH UPTX: 20040115

TECHNOLOGY FOCUS - BIOLOGY - Preferred Materials: (I) is an antibody or nucleotide. Antibodies are particularly directed against (non-)phosphorylated kinase consensus sequences, especially a Sgk1 consensus sequence in Nedd4-2, optionally mutated. In method (2), (Ia) is an activator, inhibitor, regulator and/or biological precursor of the specified proteins, particularly (a) a polynucleotide that encodes a (poly)peptide (or the (poly)peptide itself) that alters expression and/or function of the specified proteins or (b) a compound of molecular weight below 1000. The compound particularly inhibits Sgk and/or PKB, and/or stimulates at least one Nedd, for treatment of **obesity**, and is especially a kinase inhibitor, e.g. staurosporin and/or chelerythrin or their analogs and/or at least one ligase activator. (Ia) has the opposite effect when an increase in body weight is required and in this case it is a growth factor, especially insulin, insulin-like growth factor-1; a

corticoid, gonadotropin and/or cytokine, particularly transforming growth factorbeta.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Process: This may comprise detecting a mutation, especially an activating mutation in Nedd, at the DNA, RNA or protein levels, specifically a mutation in a segment that represents an Sgk1 consensus sequence, most particularly the Ser338Asp or Ser444Asp mutation in Nedd4-2. Alternatively, the mutation is activating and is present in Sgk and/or PKB, specifically Ser442Asp Sgk1 or Thr308Asp, Ser473Asp in PKB. The specified proteins can also be detected by standard immunoassays. In method (1), the polymorphism is a single nucleotide polymorphism, specifically exon8 CC/CT or intron 6 CC in sgk1. In method (7), sglt1 is overexpressed, optionally also (a) expression and/or function of at least one Sgk and/or PKB is increased (particularly overexpressed) and/or (b) expression and/or function of Nedd is reduced.

L115 ANSWER 3 OF 15 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-712756 [67] WPIX
DNN N2003-570068 DNC C2003-196094
TI Use of a novel neuropeptide receptor, designated MRGX2, for diagnosing, treating or preventing MRGX2-mediated disorder in a mammal, e.g. pain, stroke, memory disorders, diabetes, cancer, **obesity**, viral infections or depression.
DC B04 D16 S03
IN FIDOCK, M D; ROBAS, N M
PA (PFIZ) PFIZER INC; (PFIZ) PFIZER LTD
CYC 101
PI WO 2003073107 A2 20030904 (200367)* EN 58p G01N033-74
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
EP 1340979 A2 20030903 (200370) EN G01N033-74
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
US 2003171293 A1 20030911 (200382) A61K038-17
ADT WO 2003073107 A2 WO 2003-IB601 20030217; EP 1340979 A2 EP 2003-250902 20030213; US 2003171293 A1 Provisional US 2002-368448P 20020327, Provisional US 2002-422665P 20021031, US 2003-373135 20030224
PRAI GB 2002-23720 20021011; GB 2002-4610 20020227
IC ICM A61K038-17; G01N033-74
ICS A61K038-00; **A61K038-31**; C07K014-72; C12N015-00; C12N015-10
AB WO2003073107 A UPAB: 20031017
NOVELTY - Expressing a novel neuropeptide receptor, designated MRGX2, comprising:

(a) transferring an expression vector comprising a fully defined sequence of 993 bp given in the specification, or its variants or homologues, into host cells, and culturing the host cells under conditions suitable for the expression of the receptor; or

(b) upregulating the expression of MRGX2 in a suitable cell, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) screening for compounds that are modulators of a novel neuropeptide receptor MRGX2;

(2) screening for agonists or antagonists of a novel neuropeptide receptor;

(3) a compound identified using the methods of (1) or (2);

(4) a pharmaceutical composition comprising the compound of (3), and a pharmaceutical carrier;

(5) preparing a pharmaceutical composition; and

(6) diagnosing a novel neuropeptide receptor-mediated disorder in a

mammal.

ACTIVITY - Analgesic; Cerebroprotective; Nootropic; Antidiabetic; Cytostatic; Anorectic; Antidepressant; Hypotensive; Hypertensive; Cardiant; Uropathic; Antiasthmatic; Antianginal; Antiulcer; Virucide; Anti-HIV; Antiinflammatory. No biological data given.

MECHANISM OF ACTION - Gene Therapy.

USE - The neuropeptides cortistatin, somatostatin, Bam 13-22, alpha -MSH, neuropeptide FF, dynorphin A or substance P, or an analogue or mimetic of any one of these neuropeptides is useful as a ligand or modulator for receptor MRGX2, or for eliciting a functional response on receptor MRGX2 (claimed). MRGX2, its agonists and antagonists are useful for diagnosing, treating or preventing MRGX2-mediated disorder in a mammal, e.g. sleep disorders, pain, stroke, memory disorders, diabetes, cancer, **obesity**, depression, eating disorders, hypertension, hypotension, heart failure, incontinence, asthma, chronic bronchitis, angina, ulcers, viral infections including HIV-1 or HIV-2, inflammatory conditions, sexual dysfunctions, or urogenital disorders. The antibodies are useful in detecting MRGX2 in a biological sample, or as part of a diagnostic or prognostic technique.

Dwg.0/2

FS CPI EPI

FA AB; DCN

MC CPI: B04-C01C; B04-C01D; **B04-J10**; B04-K0100E; B11-C08E; B11-C10; B12-K04A1; B12-K04A2; B12-K04A4; B12-K04A5; B12-K04E; B14-A02; B14-C01; B14-C03; B14-E11; **B14-E12**; B14-F01B; B14-F01D; B14-F02A; B14-F02B; B14-F02D1; B14-H01; B14-J01A1; B14-J01A4; B14-J01B; B14-K01; B14-K01A; B14-L01; B14-N07D; B14-N16; B14-N17B; B14-S04; D05-H09; D05-H17A4

EPI: S03-E14H

TECH UPTX: 20031017

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In expressing a novel neuropeptide receptor MRGX2, the host cells are mammalian cells or insect cells. Screening for compounds that are modulators of MRGX2 comprises using cortistatin, somatostatin, Bam 13-22, alpha-MSH, neuropeptide FF, dynorphin A or substance P, or an analogue or mimetic of any one of these neuropeptides as a ligand. The method may also comprise contacting a sample of receptor MRGX2 with a ligand such as cortistatin, somatostatin, Bam 13-22, alpha-MSH, neuropeptide FF, dynorphin A or substance P, or an analogue or mimetic of any one of these neuropeptides, contacting a similar sample of receptor MRGX2 or membranes prepared from the cells with both the ligand used above and a test compound or mixture of test compounds, and comparing the results to determine whether the binding of the ligand used is affected by the presence of the test compound or mixture of test compounds. Alternatively, the method comprises contacting a sample of receptor MRGX2 with a ligand such as cortistatin, somatostatin, Bam 13-22, alpha-MSH, neuropeptide FF, dynorphin A or substance P, or an analogue or mimetic of any one of these neuropeptides with a detectable label attached, contacting a similar sample of receptor MRGX2 or membranes prepared from the cells with both the labeled ligand used above and a test compound or mixture of test compounds, and comparing the amount of label bound to determine whether the binding of the ligand used is affected by the presence of the test compound or mixture of test compounds. The sample of MRGX2 comprises cells prepared by expressing MRGX2, cells naturally expressing MRGX2, or membranes prepared from the cells, or MRGX2 protein enriched or purified from the cells or membranes. Screening for agonists of a novel neuropeptide receptor comprises adding a test compound or a mixture of test compounds to cells expressing MRGX2, and measuring whether a functional response is seen. The functional response is a transient rise in intracellular calcium concentration, acidification of the surrounding medium as measured by microphysiometry, or activation of a reporter gene linked to a cyclic AMP response element. Screening for antagonists of a novel neuropeptide receptor comprises adding a test compound or a mixture of test compounds to cells expressing

MRGX2, adding cortistatin, somatostatin, Bam 13-22, alpha-MSH, neuropeptide FF, dynorphin A or substance P, or an analogue or mimetic of any one of these neuropeptides, or an agonist identified by the method cited above, and measuring whether a functional response is seen, identifying antagonists as the test compounds which reduce the functional response to the agonist. The cells expressing MRGX2 are cells naturally expressing MRGX2, or cells produced by the method cited above. Preparing a pharmaceutical composition comprises determining whether a compound is a novel neuropeptide receptor agonist or antagonist using the method above, and admixing the compound with a pharmaceutical carrier. Diagnosing a novel neuropeptide receptor-mediated disorder in a mammal comprises measuring the level of MRGX2 gene expression, or measuring the neuropeptide-dependent activity of MRGX2 in a patient sample, and comparing the measurement to that determined from clinically normal individuals.

ABEX UPTX: 20031017

WIDER DISCLOSURE - Also disclosed are MRGX2 proteins, nucleotide sequences encoding the MRGX2 receptor, host-expression vector system expressing the nucleotide sequences, and antibodies that specifically recognize one or more epitopes of MRGX2.

ADMINISTRATION - Administration may be oral, buccal, parenteral, rectal, or by inhalation or insufflation (either through the mouth or the nose). No dosage details given.

EXAMPLE - A host cell line, e.g. HEK293 cells or Chinese hamster ovary cells, was transfected with a mammalian cell expression vector containing the cDNA encoding receptor MRGX2, and containing a selectable marker, e.g. a neomycin resistance gene. Following transfection, selection pressure was applied by adding 400-800 microg/ml G418 to the growth medium killing all cells that have not taken up the vector. After about 3-4 weeks selection, individual clones were picked and expanded for further analysis by Northern blot using a labeled probe designed from the receptor MRGX2 cDNA sequence.

L115 ANSWER 4 OF 15 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-239103 [23] WPIX
DNC C2003-061208
TI New somatostatin-dopamine chimeric analogs useful for the treatment of e.g. lung cancer.
DC B02 B04
IN CULLER, M D; DONG, Z X; KIM, S H; MOREAU, J
PA (SCRC) SCRAS SOC CONSEILS RECH & APPL SCI
CYC 100
PI WO 2002100888 A1 20021219 (200323)* EN 85p C07K007-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
ADT WO 2002100888 A1 WO 2002-US17859 20020607
PRAI US 2001-297059P 20010608
IC ICM C07K007-00
AB WO2002100888 A UPAB: 20030407
NOVELTY - Somatostatin-dopamine chimeric analogs (I) or their salts are new.

DETAILED DESCRIPTION - Somatostatin-dopamine chimeric analogs of formula (I) or their salts are new.

T = -(CH2)n-Y-(L)m-Z or C(O)-N-((CH2)n'-Y'-(L')m-Z)(C(O)-HN-R'5);
X = H, halo, CN or 1-5C alkyl;
R1 = H, 1-4C alkyl, allyl, alkenyl or CN;

R2 and R3 = H or absent;
R4 = H or CH3;
Y = Y1, Y2 or Y3;
Y1 = -S-, -S(O)-, -S(O)2-, -O-, -N(R6)-;
Y2 = -S-, -O-, -N(R6)-;
Y3 = -C(O)-, -SC(O)-, -OC(O)-, -S(CH2)s-C(O)-, -N(R5)-C(O)-;
m = 0 - 1;
n = 0 - 10;
L = -(CH2)p-C(O)- when Y=Y1, -C(O)-(CR7R8)q-C(O)- when Y=Y2 or (Doc)t when Y=Y3;
p, s and t = 1 - 10;
q = 2 - 4;
Z = somatostatin analog or a moiety comprising H, OH, 1-6C alkoxy, arylalkoxy, NH2 or NR9R10;
R5 - R10 = H or 1-5C alkyl;
R'5 = 1-5C alkyl or -(CH2)rN(CH3)q;
Y' = Y4, Y5 or Y6;
Y4 = -O-, -S-, -N(R7)-;
Y5 = -O-, -S-, -N(R7)-;
Y6 = -C(O)-, -SC(O)-, -OC(O)-, -N(R6)-C(O)-, or -N(R8)-(CH2)s-C(O)-;
r = 1 - 8;
n' = 2 - 10;
L' = -(CH2)p-C(O)- when Y'=Y4, -C(O)-(CR9R10)q-C(O)- when Y'=Y5 or -(Doc)t when Y'=Y6.

Provided that when R2 and R3 are absent a double bond is present between the carbon atoms to which they are attached.

AN INDEPENDENT CLAIM is included for eliciting a dopamine and/or a somatostatin receptor agonist effect comprising administration of a compound of formula (I).

ACTIVITY - Cytostatic; Antithyroid; Vasotropic; Anti-inflammatory; Antidiarrheic; Anti-HIV; Dermatological; Anti-diabetic; Osteopathic; Antibacterial; Immunomodulator; Hypertensive; Tranquilizer; Antilipemic; Nephrotropic; Antiulcer; Antiarthritic; Hypotensive; Anorectic; Antiaddictive.

MECHANISM OF ACTION - Dopamine receptor agonist and somatostatin receptor agonist.

Test details are described but no results are given.

USE - For the treatment of lung cancer, glioma, anorexia, hypothyroidism, hyperaldosteronism, H.pyroli proliferation, acromegaly, restenosis, Crohn's disease, systemic sclerosis, external and internal pancreatic pseudocysts and ascites, VIPoma, nesidoblastosis, hyperinsulinism, gastrinoma, Zollinger-Ellison Syndrome, diarrhea, AIDS related diarrhea, chemotherapy related diarrhea, scleroderma, irritable bowel syndrome, pancreatitis, small bowel obstruction, gastroesophageal reflux, duodenogastric reflux, Cushing's syndrome, gonadotropinoma, hyperparathyroidism, Gravas' disease, diabetic neuropathy, Paget's disease, polycystic ovary disease, thyroid cancer, hepatome, leukemia, meningioma, cancer cachexia, orthostatic, hypotension, postprandial hypotension, panic attacks, GH secreting adenomas, acromegally, TSH secreting adenomas, prolactin secreting adenomas, insulinoma, glucagonoma, diabetes mellitus, hyperlipidemia, insulin insensitivity, Syndrome X, angiopathy, proliferative retinopathy, dawn phenomenon, nephropathy, gastric acid secretion, peptic ulcer, enterocutaneous fistula, pancreaticocutaneous fistula, dumping syndrome, watery diarrhea syndrome, pancreatitis, gastrointestinal hormone secreting tumor, angiogenesis, arthritis, allograft rejection, graft vessel bleeding, portal hypertension, gastrointestinal bleeding, obesity and opioid overdose (all claimed).

ADVANTAGE - The compounds simultaneously elicit dopamine receptor agonist and somatostatin receptor agonist effects in vivo with enhanced biological activity over the native somatostatin and dopamine analogs alone.

Dwg.0/0

FS CPI
FA AB; GI; DCN
MC CPI: B04-C01B; B04-C01C; B04-C01D; **B04-J10**; B14-C03; B14-C09; B14-E02; B14-E07; B14-E08; B14-E10; B14-E11; **B14-E12**; B14-F01G; B14-F02A; B14-F06; B14-G02C; B14-H01; B14-J01B4; B14-J02C2; B14-L01; B14-M01C; B14-N01; B14-N10; B14-N11; B14-N13; B14-N14; B14-N17; B14-S04
TECH UPTX: 20030407
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) is prepared according to the methods described in WO8802756.
ABEX UPTX: 20030407
SPECIFIC COMPOUNDS - 489 Compounds are specifically claimed as (I) e.g. a compound formula (Ia).

ADMINISTRATION - (I) is administered in a dosage of 0.0001 - 100 (preferably 0.01 - 10) mg/kg orally, parenterally (including intramuscularly, intraperitoneally, intravenously or subcutaneously), through implant, nasally, vaginally, rectally, sublingually or topically.

EXAMPLE - (7-Allyl-4,6,6a,7,8,9,10,10a-octahy dro-indolo(4,3-fg)quinolin-9-ylmethylsulfanyl)-acetic acid was mixed with H-(Doc)3-D-Phe-Cys(Acm)-Tyr(tBu)-D-Trp(Boc)-Lys(Boc)-Abu-Cys(Acm)-Thr(tBu)-Rink amide MBHA resin (1 equivalent (eq.)), HBTU (2-(1-H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate) (2.9 eq.), HOBt (hydroxybenzotriazole) (3 eq.), and DIEA (diisopropylethylamine) (6 eq.) in DMF. The resulting mixture was worked up to form a compound of formula (Ia).

L115 ANSWER 5 OF 15 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-147883 [14] WPIX
DNC C2003-038100
TI New method of treating **obesity**, reducing caloric intake or inhibiting insulin hypersecretion in an **obese** adult, comprises administering somatostatin, its receptor agonist and/or salt to a patient exhibiting primary insulin hypersecretion.
DC B04
IN LUSTIG, R H
PA (LUST-I) LUSTIG R H
CYC 1
PI US 2002156010 A1 20021024 (200314)* 18p A61K038-31 <--
ADT US 2002156010 A1 Provisional US 2000-252324P 20001120, US 2001-6738 20011108
PRAI US 2000-252324P 20001120; US 2001-6738 20011108
IC ICM **A61K038-31**
AB US2002156010 A UPAB: 20030227
NOVELTY - New method (M) of treating **obesity**, reducing caloric intake or inhibiting insulin hypersecretion in an **obese** adult patient (P), comprises administering to (P) exhibiting primary insulin hypersecretion, an effective amount of somatostatin or its receptor agonist, its salt or their combinations.
DETAILED DESCRIPTION - New method (M) of treating **obesity**, reducing caloric intake or inhibiting insulin hypersecretion in an **obese** adult patient (P), comprises administering to (P) exhibiting primary insulin hypersecretion, an effective amount of somatostatin or its receptor agonist, its salt or their combinations under conditions effective to reduce weight, caloric intake and insulin secretion by pancreatic beta -cells of (P), respectively.
ACTIVITY - Anorectic.
MECHANISM OF ACTION - Inhibitor of insulin secretion (claimed).
Subjects were treated with six injections of octreotide-LAR. 40 mg IM q28 d from weeks 0-20, given as two intragluteal 20 mg injections. Subjects were also treated with ursodeoxycholic acid. 600 mg PO qd to prevent cholelithiasis. Subjects were allowed to eat ad libitum, and

neither dietary nor exercise interventions were recommended. Subjects checked their capillary blood glucose (CBG), three times a week, both before and 2 hr after a meal. Individual values were down-loaded, and monthly averages of CBG were calculated at each visit to evaluate excursions of glucose in response to normal dietary intake. 53 subjects were recruited. Nine subjects (17%) dropped out during the study, 4 due to lack of weight loss during the first 4-20 weeks, and 5 for other reasons. 44 subjects completed the 24 weeks. Analysis of gender (5M, 39F) demonstrated no differences in response to octreotide. Impaired glucose tolerance (IGT) was present in 14 subjects (32%). Seven subjects (16%) were receiving thyroxine supplementation. Weight, body mass index (BMI) and WHR were decreased by octreotide-LAR therapy in the entire cohort. Weight decreased by 3.6 plus or minus 0.9 kg, BMI decreased by 1.2 plus or minus 0.1 kg/m2, and WHR decreased by 0.02 plus or minus 0.01. The magnitude of response was very broad. High response (HR) subjects lost 12.6 plus or minus 1.1 kg and BMI of -4.4 plus or minus 0.4, low response (LR) subjects lost 3.6 plus or minus 0.4 kg and BMI of -1.3 plus or minus 0.2, and NR gained 3 kg and BMI of 1.2 plus or minus 0.3. The Caucasian population lost 4.7 plus or minus 1.2 kg and BMI of -1.5 plus or minus 0.4, and the minority population lost 1.8 plus or minus 1.2 kg and BMI of -0.6 plus or minus 0.4, but the difference between the races was not significant. The C-peptide curves from the oral glucose tolerance test (OGTT) at week 0 were indistinguishable among response strata, but their insulin curves were highly dissimilar. The HR insulin curve had a rapid ascending limb with a sharp peak, followed by a rapid decline. The no response (NR) insulin curve had a slow ascending limb with a plateau between 60 and 150 minutes. The LR insulin curve had components of both HR and NR curves, with a lack of an acute peak but with a shorter plateau. After 24 weeks of octreotide-LAR therapy, C-peptide suppression was evident only in HR and LR. Similarly, the insulin response was suppressed in HR and LR. C-peptide curves were indistinguishable between races at both time points, however, Caucasians demonstrated decreased insulin responses versus minorities, both at week 0 and week 24.

USE - (M) is useful for treating **obesity** in adult patients, reducing the caloric intake in an **obese** adult patient, and for inhibiting insulin hypersecretion in an **obese** adult patient, e.g. human (claimed).

ADVANTAGE - Inhibiting insulin secretion using the somatostatin analog octreotide, results in effective loss of weight and fat mass.

Dwg.0/5

FS CPI

FA AB; DCN

MC CPI: B04-C01B; B04-C01C; B04-H06H; **B14-E12**; B14-L06

TECH UPTX: 20030227

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The somatostatin receptor agonist is a somatostatin analog, e.g. octreotide or **lanreotide**.

The somatostatin receptor agonist is an agonist of somatostatin receptor type 2 or receptor type 5.

ABEX UPTX: 20030227

ADMINISTRATION - 1-100 microg/kg/day, preferably 20-60 mg/month of somatostatin, its receptor agonist or salt is administered through intramuscular or subcutaneous route (claimed). The compounds are also administered through transdermal, parenteral, intravenous or intraarterial route.

L115 ANSWER 6 OF 15 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2003-129486 [12] WPIX

DNN N2003-102804 DNC C2003-033223

TI Expressing a desired active or pharmaceutical agent, e.g. a hormone in a host for treatment or replacement therapy, comprises administering transduced stem cells having a desired gene under control of cell-type specific promoter.

DC B04 B05 D16 P14
IN BOYLAN, M O; JEPEAL, L I; WOLFE, M M; JEPEAL, L
PA (BOYL-I) BOYLAN M O; (JEPE-I) JEPEAL L I; (WOLF-I) WOLFE M M; (ENTE-N) ENTEROMED INC
CYC 100
PI WO 2002096195 A1 20021205 (200312)* EN 45p A01K067-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
US 2003157071 A1 20030821 (200356) A61K048-00
ADT WO 2002096195 A1 WO 2002-US17178 20020531; US 2003157071 A1 Provisional US 2001-294772P 20010531, US 2002-161256 20020531
PRAI US 2001-294772P 20010531
IC ICM A01K067-00; A61K048-00
ICS A01K067-027; A01N043-04; A01N063-00; A01N065-00; A61K031-70; C12N005-00; C12N005-02; C12N005-08
AB WO 200296195 A UPAB: 20030218
NOVELTY - Selectively (M) expressing a desired active or pharmaceutical agent in a host, comprises:

(a) transducing a population of stem cells with a DNA sequence containing a gene encoding the desired active or pharmaceutical agent, operably-linked to a cell type specific promoter;

(b) administering the transduced stem cells to a host; and

(c) allowing the cells to express the desired gene.

DETAILED DESCRIPTION - Selectively (M) expressing a desired active or pharmaceutical agent in a host, comprises:

(a) transducing a population of stem cells with a DNA sequence containing a gene encoding a desired active or pharmaceutical agent, where the gene is operably-linked to a cell type specific promoter;

(b) administering the transduced stem cells to a host under conditions where some of the stem cells differentiate into cells of the type the cell type specific promoter is specific for (referred to, as differentiated stem cells); and

(c) allowing the differentiated stem cells to express the desired active or pharmaceutical agent in the host.

INDEPENDENT CLAIMS are also included for the following:

(1) differentiated transduced stem cells delivered to the gut of a host for attaching to the gut and selectively expressing a desired active or pharmaceutical agent while engrafted in the intestine, the differentiated transduced stem cells comprising:

(a) a DNA sequence containing a gene encoding the desired active or pharmaceutical agent; and

(b) a cell type specific promoter which is specific for the differentiated transduced stem cells, where the differentiated transduced stem cells, while engrafted in the intestine, have the ability to express the desired active or pharmaceutical agent; and

(2) a population of transduced stem cells suitable for engrafting in the intestine of a host and differentiating once engrafted for selectively expressing a desired active or pharmaceutical agent comprising a population of stem cells transduced with a DNA sequence containing a gene encoding a desired active or pharmaceutical agent, operably-linked to a cell type specific promoter, where some of the population of stem cells, once engrafted in the intestine of a host, have the ability to differentiate into cells of the type for which the cell type specific promoter is specific and express the desired active or pharmaceutical agent.

ACTIVITY - Antidiabetic; Anorectic; Antiulcer; Cytostatic; Hepatotropic; Neuroprotective; Vasotropic; Hypotensive; Antidiarrheic; Hemostatic; Antiviral; Antiaging.

MECHANISM OF ACTION - Cell therapy; Hormone therapy. To determine where the glucose-dependent insulinotropic polypeptide (GIP)/Ins transgene can specifically target expression of human insulin to gut K cells in vivo, transgenic mice were generated by injecting the linearized GIP/Ins fragment into pronuclei of fertilized mouse embryos. In the resulting transgenic mice, human insulin was expressed in duodenum and stomach, but not in other tissues examined. Plasma levels of human insulin in pooled samples collected after an oral glucose challenge were 39.0 plus or minus 9.8 pM in transgenic and undetectable in controls. Amounts of mouse C peptide after an oral glucose load in transgenics were 30 % lower than those of controls. This observation suggested that human insulin produced from the gut led to compensatory down-regulation of endogenous insulin production. Whether human insulin production from gut K cells was capable of protecting transgenic mice from diabetes was investigated. Streptozocin (STZ), a (beta)-cell toxin, was administered to transgenic mice and age-matched controls. In control animals, STZ treatment resulted in fasting hyperglycemia (26.2 plus or minus 1.52 mM) and the presence of glucose in the urine with 3 to 4 days, indicating the development of diabetes. When left untreated, these animals deteriorated rapidly and died within 7 - 10 days. In contrast neither glucosuria nor fasting hyperglycemia (9.52 plus or minus 0.67 mM) was detected in transgenic mice for up to 3 months after STZ treatment, and they continue to gain weight normally. To determine whether insulin production from K cells was able to maintain oral glucose tolerance in these mice, despite the severe beta -cell damage by STZ, mice were challenged with an oral glucose load. Control mice given STZ were severely hyperglycemic both before and after the glucose ingestion. In contrast, STZ-treated transgenic mice had normal blood glucose levels and rapidly disposed of the oral glucose load as did normal age-matched control mice. To ensure that the STZ treatment effectively destroyed the beta -cells in these experimental animals, pancreatic sections from controls and STZ-treated transgenic animals were immunostained from mouse insulin. The number of cell clusters positively stained for mouse insulin was substantially lower in STZ-treated animals when compared with sham-treated controls. These STZ-treated transgenic mice disposed of oral glucose in the same way that normal mice did, despite having virtually no pancreatic beta -cells, which indicated that human insulin produced from the gut was sufficient to maintain normal glucose tolerance.

USE - (M) is useful for selectively expressing a desired active or pharmaceutical agent such as a protein, peptide, enzyme, hormone, hormone synthesis enzyme, pro-drug and precursor in a host. The active or pharmaceutical agent is interferon, a hormone, an enzyme, somatostatin, anti-GIP (glucose-dependent insulinotropic polypeptide), an interleukin, a chemokine, a cytokine, erythropoietin (EPO), nitric oxide, synthetase, a clotting factor, thrombin and pro-thrombin. The active or pharmaceutical agent is especially a hormone such as insulin, estrogen, testosterone, luteinizing hormone, follicle stimulating hormone, prolactin, leptin, or angiotensin. The method is especially useful for expressing a hormone in a host, or for treating or replacing a hormone in the host who has a hormone deficiency condition such as type I diabetes, type II diabetes, hypogonadism, reproductive disorders, and **obesity** (claimed). The method is also useful for treating acquired immunodeficiency syndrome (AIDS)-diarrhea, gastrointestinal bleeding, peptic ulcers, cancer, hepatitis, multiple sclerosis, melanoma, aging, erectile dysfunction, GI motility disorders, vascular tone and hypertension.

ADVANTAGE - Stem cells are transduced ex vivo with high efficiency and the cell type specific promoter insures that the desired active or pharmaceutical agent is expressed by a desired cell type.

Dwg.0/3

FS CPI GMPI

FA AB; DCN

MC CPI: B01-C05; B04-E03; B04-E04; B04-F0100E; B04-F0400E; B04-H0100E; B04-H0200E; B04-H0500E; B04-H0700E; B04-H1900E; B04-J0100E;

B04-J03A0E; B04-J1000E; B04-J1800E; B04-L0100E; B04-L0800E; B04-N0400E; B05-C03; B14-A02; B14-D01; B14-E02; B14-E08; **B14-E12**; B14-F02; B14-F02A; B14-F08; B14-H01; B14-N07; B14-N12; B14-N17; B14-S01; B14-S04; D05-C03; D05-C12; D05-H08; D05-H12A; D05-H17A

TECH UPTX: 20030218

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The stem cells are bone marrow derived stem cells, embryonic stem cells, adipose tissue derived stem cells, and cord blood cells. The tissue specific promoter is glucose-dependent insulinotropic polypeptide (GIP). The stem cells differentiate into K cells of the gut. The stem cells are further transduced with a killer gene under the control of a regulatable promoter, where the induction of the expression of the killer gene results in cell death of the cell expressing the gene. The killer gene is the fas ligand.

ABEX UPTX: 20030218

ADMINISTRATION - The stem cells are administered to the host by infusion into the superior mesenteric artery or celiac artery or by injection into the intestinal mucosa in a pharmaceutical excipient such as physiological buffer or saline or glucose solution compatible with the transduced stem cells (claimed). 105 - 1013 cells/100 kg person are administered per infusion, preferably 1 - 5 x 108 to 1 - 5 x 1012 cells are infused intravenously/100 kg person.

L115 ANSWER 7 OF 15 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-060753 [06] WPIX
DNC C2003-015999
TI Vaccine for oral and transmucosal administration useful e.g. in prevention and treatment of bacterial, viral, mycotic and parasitic infections comprises antigens conjugated with lectins and coated with polysaccharide.
DC A96 B04 C06 D16
IN BIZZINI, B; VOLPATO, I; WYSS, R
PA (GRIS-N) GRISOTECH SA; (BIZZ-I) BIZZINI B; (VOLP-I) VOLPATO I; (WYSS-I) WYSS R
CYC 28
PI EP 1243256 A1 20020925 (200306)* EN 26p A61K009-16
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2002326953 A 20021115 (200306) 22p A61K039-00
US 2003049279 A1 20030313 (200321) A01N037-18
ADT EP 1243256 A1 EP 2002-6076 20020318; JP 2002326953 A JP 2002-77103 20020319; US 2003049279 A1 US 2002-101034 20020318
PRAI IT 2001-MI571 20010319
IC ICM A01N037-18; A61K009-16; A61K039-00
ICS A61K009-00; A61K038-00; A61K039-002; A61K039-02; A61K039-08; A61K039-106; A61K039-112; A61K039-12; A61K039-145; A61K039-20; A61K039-245; A61K039-25; A61K039-35; A61K039-385; A61K039-39; A61K045-00; A61K047-00; A61K047-36; A61K047-48; A61P001-04; A61P003-02; **A61P003-04**; A61P003-06; A61P015-00; A61P019-10; A61P031-04; A61P031-10; A61P031-12; A61P033-00; A61P037-08; A61P039-00; A61P043-00; C12N001-20
ICI C12N001-20; C12R001:15
AB EP 1243256 A UPAB: 20030124

NOVELTY - Vaccines comprising antigens conjugated with lectins and coated with polysaccharide, are new.

DETAILED DESCRIPTION - Vaccines comprising antigens conjugated with lectins and coated with polysaccharide; lectins direct the antigens to mucosal cells enabling efficient oral and transmucosal administration, whilst the polysaccharide isolates lectins from non-specific and potentially toxic absorption, protects the antigen from degradation due to proteolytic enzymes and the gastric environment and possibly has an immunostimulating effect.

INDEPENDENT CLAIMS are also included for:

(1) a delipidated Corynebacterium granulosum fraction incorporated in

polysaccharides for use as in immunoadjuvant with vaccines as above; and
(2) producing vaccines and delipidated Corynebacterium granulosum fraction as in (1).

USE - The vaccines are useful in prevention and treatment of bacterial, viral, mycotic and parasitic infections (claimed) and to prepare drugs to treat such infections. They can be administered orally and transmucosally (e.g. by buccal, rectal or nasal administration) (claimed) and may be included in solid and liquid food supplements for humans or other animals (claimed). They may also be used to produce medicaments to treat narcotics overdose syndrome, osteoporosis, ulcers, hypercholesterolemia, **obesity**, infertility, delipidated or allergies or to treat/prevent growth-related disorders. The vaccines may be included with adjuvants (especially the claimed delipidated Corynebacterium granulosum fraction incorporated in polysaccharides) and/or excipients in compositions (claimed), especially compositions for oral and/or transmucosal administration (claimed).

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: A03-A01; A12-V01; B04-C02; B04-F10; B04-F11; B04-J01; B04-L01; B04-N04; B14-A01; B14-A02; B14-A04; B14-B02; **B14-E12**; B14-F06; B14-G02A; B14-N01; B14-N17B; B14-P02; B14-S11; C04-C02; C04-F10; C04-F11; C04-J01; C04-L01; C04-N04; C14-A01; C14-A02; C14-A04; C14-B02; **C14-E12**; C14-F06; C14-G02A; C14-N01; C14-N17B; C14-P02; C14-S11; D05-H07

TECH UPTX: 20030124

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Vaccines: The polysaccharide is preferably chitosan, low-molecular-weight and high-deacetylation-degree chitosan, methyl glycol chitosan, alginic acid, polymannuronic acid or salts/derivatives of one of these. It is preferably not chemically cross-linked to conjugated antigen e.g. linked by non-covalent bonds such as ionic bonds. Antigens are preferably selected from: microorganisms; infectious agents or their constituents (e.g. Herpes simplex virus, cytomegalovirus etc.); hormones (especially chorionic gonadotropin, parathormone, glucagon or thyroid hormone); enzymes and proenzymes; narcotics (especially cocaine, heroin, lysergic acid (LSD) or their derivatives); bioactive peptides (especially somatostatin, cholecystokinin or calcitonin); metabolites; physiological precursors; cell constituents (especially cholesterol); and allergens (especially Poa pratensis). Lectins are preferably of vegetable origin e.g. from Lens culinaris, Glycine max, or Phaseolus vulgaris. They are preferably chemically conjugated to antigen, especially by reaction between the aldehydic and aminate groups. The delipidated Corynebacterium granulosum fraction incorporated in polysaccharides preferably uses preferred polysaccharides as above (preferably not chemically cross-linked); it is preferably for oral or mucosal use.

ABEX UPTX: 20030124

ADMINISTRATION - Vaccine may be administered orally and transmucosally. No dosage details given.

EXAMPLE - Several different antigens were conjugated with commercially available lectins e.g. Salmonella enteritidis antigen was conjugated with a lectin from Lens culinaris by standard methods. Conjugated antigens were then incorporated into polysaccharides chitosan or alginic acid. For example, chitosan was dissolved in 0.025 M acetate buffer (pH 5.7) and conjugated antigen solution dissolved in 0.05 M Na2SO4 (10 mg/2.5 ml); solutions were heated to 55degreesC, chitosan solution (2.5 ml) added to conjugated antigen solution (2.5 ml) and mixture vortexed (maximum speed, 20-60 sec.). Rabbits (n=20) were administered vaccine as above according to two vaccination schemes (with/without sensitization step) as detailed in the specification. Antibody production was measured 15 days after last booster dose by known enzyme linked immunosorbent assay (ELISA) assay, and compared with that in Controls and in animals treated with antigen

non-conjugated with lectins but incorporated in chitosan. Results (given in the specification) demonstrated that the vaccine induced antibody production using both vaccination protocols, and that vaccine was more effective than vaccine comprising antigen non-conjugated with lectins.

L115 ANSWER 8 OF 15 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-351844 [38] WPIX
DNC C2002-099958
TI Sustained release composition to treat central nervous system disorders comprises a water insoluble complex of a peptide and ligands, and a carrier macromolecule.
DC B04
IN GEFTER, M L
PA (PRAE-N) PRAECIS PHARM INC
CYC 97
PI WO 2002022154 A2 20020321 (200238)* EN 35p A61K038-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
US 2002086829 A1 20020704 (200247) A61K038-16
AU 2001089079 A 20020326 (200251) A61K038-00
ADT WO 2002022154 A2 WO 2001-US28691 20010913; US 2002086829 A1 Provisional US 2000-232188P 20000913, US 2001-953247 20010913; AU 2001089079 A AU 2001-89079 20010913
FDT AU 2001089079 A Based on WO 2002022154
PRAI US 2000-232188P 20000913; US 2001-953247 20010913
IC ICM A61K038-00; A61K038-16
AB WO 200222154 A UPAB: 20020618
NOVELTY - A sustained release composition (I) comprises a water insoluble complex (WIC) of a peptide (II) and ligands (III) which are linked.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a composition comprising a water insoluble complex (WIC) of a peptide (II), ligands (III), each being negatively or positively charged, and an ionic carrier macromolecule (IV) linked to (III) having a charge opposite to the charge of (III);

(2) a composition comprising WIC of a peptide (II), ligands (III), each being positively charged, and carboxymethylcellulose;

(3) a composition comprising WIC of a charged active drug, and an ionic (IV) having a charge opposite to the charge of the drug; and

(4) preparation of the compositions.

ACTIVITY - Nootropic; Neuroprotective; Antiparkinsonian; Anticonvulsant; Hypotensive; Antidepressant; Tranquilizer; Antimigraine; Anorectic; Antiarteriosclerotic; Antiangial; Cytostatic; Antidiabetic; Antithyroid; Antiulcer; Antiinflammatory; Anti-HIV; Immunosuppressive; Nephrotropic.

MECHANISM OF ACTION - None given in the source material.

USE - The sustained delivery of peptides are used to treat central nervous system disorders, e.g. Alzheimer's disease, Parkinson's disease, multiple sclerosis, epilepsy, autonomic function disorders, e.g. hypertension, neuropsychiatric disorders, e.g. depression, anxiety, learning or memory disorders, e.g. amnesia, attention deficit disorder, migraine and **obesity**, cardiovascular disorders, e.g. arteriosclerosis, angina, cancer, diabetes mellitus, thyroid disorders, reproductive disorders, inflammatory or immune system disorders, e.g. ulcerative colitis, Crohn's disease, HIV, autoimmune disorders, gastrointestinal disorders and digestive disorders, e.g. peptic ulcers, metabolic disorders, and renal disorders, e.g. glumerulonephritis.

ADVANTAGE - The association of the peptide and ligands in a tight, stable complex allows for loading of high concentrations of peptide into

the composition. The compositions also provide delivery of a peptide for prolonged periods of time, e.g. 1 month.
Dwg.0/2
FS CPI
FA AB; DCN
MC CPI: B04-C01B; B04-C02; B04-C03B; B04-H07; B04-J01; B04-J03; B04-J04; B04-J05; B04-J06; B04-J07; B04-J11; B04-J12; B04-J18; B12-M10A; B14-A02B1; B14-C01; B14-E08; B14-E10C; **B14-E12**; B14-F01D; B14-F02B; B14-F07; B14-G02D; B14-H01B; B14-J01A1; B14-J01A3; B14-J01A4; B14-J01B4; B14-J07; B14-L06; B14-N10; B14-N11; B14-P02; B14-S01; B14-S04
TECH UPTX: 20020618
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The ligands are linked directly, covalently, via electrostatic interaction, hydrophobic interaction, or a carrier macromolecule (linked covalently, electrostatically or hydrophobically).
The composition provides sustained release of the peptide for at least 2 weeks, preferably at least 4 weeks.
Preferred Peptides: The peptide is insulin, erythropoietin, growth hormone, bradykinin, parathyroid hormone, adenocorticotrophic hormone, calcitonin, vasopressin, angiotensin, desmopressin, luteinizing hormone-releasing hormone, somatostatin, glucagon, somatomedin, oxytocin, gastrin, secretin, melanocyte stimulating hormone, beta-endorphin, enkephalin, neurotensin, thyroid releasing hormone, or macrophage stimulating factor, particularly an LHRH analog, preferably LHRH antagonist (Ac-D-Nal-4-Cl-D-Phe-Pal-Ser-N-Me-Tyr-D-Asn-Leu-Lys(iPr)-Pro-D-Ala or Cetrorelix (Ac-D-Nal-4-Cl-D-Phe-Pal-Ser-Tyr-D-Cit-Leu-Arg-Pro-D-Ala)) or an agonist Leuprolide (pGlu-His-Trp-Ser-Tyr-D-Leu-Leu-Arg-Pro(ethylamide)-Gly).
Preferred Carrier: The carrier macromolecule is a derivative or fragment of an anionic polyalcohol, an anionic polysaccharide or a carboxymethylcellulose, preferably poly-allylamine, -vinylamine or -ethyleneimine, each optionally N-alkylated.
Preferred Preparation: The peptide and ligands are combined to form a complex using aseptic procedures. The complex is preferably sterilized by gamma irradiation or electron beam irradiation.
ABEX UPTX: 20020618
ADMINISTRATION - Peptide dosage of 0.001-15 mg/kg is administered by conventional routes, preferably parenteral.

EXAMPLE - A peptide ligand to human growth hormone (hGH) was isolated and the sequence determined. The ligand was synthesized with an additional 10 amino acid residue cationic sequence at the N- or C-terminus of the ligand, to form a modified ligand. hGH and the modified ligand were combined in aqueous solution in the presence of carboxymethylcellulose, precipitating a solid complex comprising hGH, modified ligand and carboxymethylcellulose.

L115 ANSWER 9 OF 15 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-206179 [26] WPIX
DNC C2002-063210
TI Novel modified biological peptide with increased biological potency, prolonged activity, increased half-life, for treating glucose intolerance associated or not with insulin resistance pathologies, type II diabetes.
DC B04 B05
IN ABRIBAT, T; GRAVEL, D; HABI, A
PA (THER-N) THERATECHNOLOGIES INC; (ABRI-I) ABRIBAT T; (GRAV-I) GRAVEL D; (HABI-I) HABI A
CYC 97
PI WO 2002010195 A2 20020207 (200226)* EN 77p C07K014-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK

DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001079526 A 20020213 (200238) C07K014-00
EP 1305338 A2 20030502 (200331) EN C07K014-605
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR
US 2003204063 A1 20031030 (200372) C07K014-61
CN 1454214 A 20031105 (200408) C07K014-605

ADT WO 2002010195 A2 WO 2001-CA1119 20010802; AU 2001079526 A AU 2001-79526 20010802; EP 1305338 A2 EP 2001-957662 20010802, WO 2001-CA1119 20010802; US 2003204063 A1 WO 2001-CA1119 20010802, US 2003-343654 20030303; CN 1454214 A CN 2001-813865 20010802

FDT AU 2001079526 A Based on WO 2002010195; EP 1305338 A2 Based on WO 2002010195

PRAI US 2000-222619P 20000802; US 2003-343654 20030303

IC ICM C07K014-00; C07K014-605; C07K014-61
ICS A61K038-04; C07K014-47; C07K014-635; C07K014-655

AB WO 200210195 A UPAB: 20020424

NOVELTY - A modified biological peptide (I) with increased biological potency, prolonged activity and/or increased half-life, and any isomers, including cis and trans configurations, epimers, enantiomers, diastereoisomers, and racemic mixtures, where the peptides defined in claim 1 of US 6020311 is excluded, is new.

DETAILED DESCRIPTION - A modified biological peptide of formula Xn-R1 (I) with increased biological potency, prolonged activity and/or increased half-life, and any isomers, including cis and trans configurations, epimers, enantiomers, diastereoisomers, and racemic mixtures, where the peptides defined in claim 1 of US 6020311 is excluded, is new.

R1 = a peptide sequence, a functional analog or its fragment;

X = identical or independent from the others, is constituted by conformationally rigid moieties, and is selected from straight, substituted (1-10)C alkyl, a branched, substituted (1-10)C alkyl, a straight or branched, unsubstituted or substituted (1-10)C alkene, a straight or branched, unsubstituted or substituted (1-10)C alkyne, an unsubstituted or substituted saturated or unsaturated (3-10)C cycloalkyl or heterocycloalkyl where the heteroatom is O, S or N, and an unsubstituted or substituted (5-14)C aryl or heteroaryl where the heteroatom is O, S or N, where the substituents comprise one or more straight or branched (1-10)C alkyl, straight or branched (1-6)C alkene, straight or branched (1-6)C alkyne, (3-10)C cycloalkyl or heterocycloalkyl where at least 2 carbon atoms are optionally connected to the (1-10)C alkyl, (1-10)C alkene, (1-10)C alkyne, (3-10)C cycloalkyl or heterocycloalkyl, and (5-14)C aryl or heteroaryl, or (5-14)C aryl or heteroaryl where at least 2 carbon atoms of the aryl or heteroaryl are optionally connected to the (1-10)C alkyl, (1-10)C alkene, (1-10)C alkyne, (3-10)C cycloalkyl or heterocycloalkyl, and (5-14)C aryl or heteroaryl, or X also comprises at least one group selected from a carboxy or an amino group for coupling with the peptide sequence by an amide bond at the N-terminal of the peptide sequence, the C-terminal of the peptide sequence, at an available carboxy or amino site on the peptide sequence chain and their combinations, and a carboxy group for coupling with the peptide sequence by an ester bond at an available hydroxy site on the peptide sequence chain, and their combinations; and

n = 1-5.

ACTIVITY - Antidiabetic; Osteopathic; Cytostatic; Antiinflammatory; Anorectic; Nootropic.

Six-week old female CDI mice were fasted for at least 16 hours. Mice were given 1.5 mg of glucose/g of body weight orally in water through a gastric gavage tube and blood was collected from a tail vein for measurement of blood glucose using a glucose meter. Peptides or vehicle were injected subcutaneously 5 minutes prior to the glucose administration. All peptides, including wild-type glucagon-like peptide

GLP-1 (7-37), were tested at different concentrations: 1, 5 and 10 micro g/mouse. In a first set of experiments, a peptide 1 ((hexenoyl-trans-3-His7)-hGLP-1 (7-37)) was tested in comparison with vehicle and hGLP-1 (7-37). In a second set of experiments, peptides 2 ((O-Tolylacetic acid-His7)-hGLP-1 (7-37)) and 3 ((+/-)-cis-2-ethylcyclopropylacetic acid-His7)-hGLP-1 (7-37)) were tested in comparison with vehicle and hGLP-1 (7-37). In the two studies, administration of vehicle resulted in a similar integrated response in glucose levels. Although GLP-1 induced a dose-related decrease in the glucose response, this peptide was not able to completely suppress the glucose response at any dose, which was interpreted as a limitation in its potential clinical usefulness. In contrast, peptide 1 completely abolished the glucose response, but only at the 10 micro g dose. Surprisingly, peptide 3 was even more potent than peptide 1, and totally prevented the glucose response both at the 5 micro g and the 10 micro g doses. In conclusion, the GPL-1 analog corresponding to peptide 3 was identified with marked increased biological potency over the wild type GLP-1 (7-37), and because of this increased potency, this peptide had clinical usefulness in treating states of insulin resistance associated with pathologies such as type II diabetes.

MECHANISM OF ACTION - Blood glucose regulator; enhancer of mucosal regeneration in patients with intestinal diseases; regulator of myometrial contractility and prostoglandin release; stimulator of ACTH release; inhibitor of interleukin-8 production; stimulator of acid release; modulator of melanocyte information process, involved in pressure and volume homeostasis; regulator of exocrine and endocrine secretions, smooth muscle contraction, feeding, blood pressure, blood glucose, body temperature, cell growth, food intake and energy balance; inhibitor of cancer cell growth; stimulator of pancreatic secretion or cell growth.

USE - (I) Is useful in the treatment of glucose intolerance associated or not with insulin resistance pathologies, and in the treatment of type II diabetes (claimed). (I) Is useful for treating bone diseases such as osteoporosis, cancer, diseases related to inflammatory responses, **obesity**, autism, pervasive developmental disorders, hyperproliferative skin diseases, hormone-dependent diseases and conditions including hormone-dependent cancers, for regulating blood glucose, to enhance mucosal regeneration in patients with intestinal diseases, for altering the proliferation of peripheral blood mononuclear cell, regulation of myometrial contractility and prostoglandin release, stimulation of ACTH release, inhibition of interleukin-8 production, stimulation of acid release, modulation of melanocyte information process, involved in pressure and volume homeostasis, regulation of exocrine and endocrine secretions, smooth muscle contraction, feeding, blood pressure, blood glucose, body temperature and cell growth, regulation of food intake and energy balance, inhibition of cancer cell growth and stimulation of pancreatic secretion or cell growth.

ADVANTAGE - (I) Is a modified biological peptide and has increased biological potency, prolonged activity and/or increased half-life (claimed).

Dwg.0/2

FS CPI

FA AB; DCN

MC CPI: B04-C01; B04-J01; B04-J04; B04-J05; B04-J06; B04-J07; B04-J08; B04-J09; **B04-J10**; B04-J11; B04-J12; B04-J14; B04-L01; B04-N02; B14-C03; B14-D01; B14-D02; **B14-E12**; B14-F09; B14-F10; B14-H01B; B14-J05; B14-N01; B14-N17C; B14-S04

TECH UPTX: 20020424

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Peptide: (I) Is selected from growth hormone releasing factor (GRF), somatostatin, glucagon-like peptide 1 (GLP-1) (7-37), amide human (GLP-1) hGLP-1 (7-36) NH2, parathyroid hormone fragments (PTH 1-34), adrenocorticotropic hormone (ACTH), osteocalcin, calcitonin, corticotropin releasing factor, dynorphin A, beta-endorphin, big gastrin-1, GLP-2, luteinizing hormone-releasing hormone, melanocyte stimulating hormone (MSH), atrial natriuretic peptide,

neuromedin B, Human neuropeptide Y, human orexin A, Human peptide YY, human secretin, vasoactive intestinal peptide (VIP), antibiotic peptides (magainin 1, magainin 2, cecropin A, and cecropin B), substance P (SP), beta casomorphin-5, endomorphin-2, procolipase, enterostatin, gastric inhibitory peptide, chromogranin A, vasostatin I and II, procalcitonin, ProNCT, calcitonin gene related peptide (CGRP), IL8 (monocyte-derived), GCP-2, PF4, IP-10, MIG, SDF-1alpha, GRO-alpha, I-TAC, RANTES, LD78, MIP-1alpha, MCP-1, MCP-2, MCP-3, MCP-4, eotaxin, MDC, and its functional analogs, derivatives or fragments, where the peptides have sequences given in the specification. The peptide sequence is a sequence of a natural peptide and its functional analog or its fragment or a clinically safe and acceptable derivative or analog. The peptide sequence is preferably somatostatin and at least one conformationally rigid moiety is coupled with the somatostatin peptide sequence by an amide bond at different positions such as position Ala1, Asp5, Cys or Ala1+Cys14. The peptide sequence is preferably PTH 1-34 and at least one conformationally rigid moiety is coupled with the PTH 1-34 sequence by an amide bond at different positions such as Ser1, Glu4, Lys26, Lys27, Asp30, or Ser1+Lys27. The peptide sequence is preferably GLP-1 and at least one conformationally rigid moiety is coupled with the GLP-1 peptide sequence by an amide bond at different positions such as His1, Glu3, Asp9, His1+Glu3, His1+Asp9, or Glu3+Asp9. The other peptide sequences such as GLP-2, enterostatin, NPY, NPYY, secretin, VIP, gastrin inhibitory peptide, vasostatin II, RANTES, CGRP and eotaxin are coupled with at least one conformationally rigid moiety by an amide or ester bond at different positions of the peptide sequences. The conformationally rigid moiety is coupled with the peptide by an amide or ester bond at the N-terminal.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) Is prepared by standard solid phase synthesis.

ABEX UPTX: 20020424

ADMINISTRATION - Administration of (I) is intravenous, intradermal, subcutaneous, transdermal, intraperitoneal, oral, topical, or by inhalation. No dosage given.

EXAMPLE - Human glucagon-like peptide (hGLP-1) (7-37) analog synthesis was as follows: hGLP-1 (7-37) derivatives modified at the amino terminus with rigid hydrophobic moieties were synthesized using Fmoc chemistry. Fmoc-Gly-Wang resin and 5 equivalents of reagents were used with a time coupling of 30 minutes. The reactions were monitored by the Kaiser test. The three conformationally rigid moieties introduced at the N-terminus of the hGLP-1 (7-37) were: O-Tolylacetic acid-His7)-hGLP-1 (7-37), and (+,-)-cis-2-ethylcyclopropylacetic acid-His7)-hGLP-1 (7-37) (+,-)-cis-2-ethylcyclopropylacetic acid. The peptides were cleaved using a trifluoroacetic acid (TFA) cocktail for 2 hours. All the analogs were purified by reverse-phase high pressure liquid chromatography (HPLC), and analyzed by analytical HPLC and by MS (Matrix-assisted laser desorption ionization-time of flight (MALDI-TOF)).

L115 ANSWER 10 OF 15 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-570911 [65] WPIX
DNC C2001-169825
TI Use of glycogen phosphorylase for the manufacture of a medicament for the treatment of diabetic cardiomyopathy.
DC B02
IN TREADWAY, J L
PA (PFIZ) PFIZER PROD INC; (TREA-I) TREADWAY J L
CYC 33
PI AU 2001016399 A 20010726 (200165)* 86p A61K031-404
CA 2331847 A1 20010724 (200165) EN A61K031-404
JP 2001206856 A 20010731 (200165) 35p A61K045-00
EP 1125580 A2 20010822 (200173) EN A61K031-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT

RO SE SI TR.
US 2001046958 A1 20011129 (200202) A61K031-405
KR 2001083148 A 20010831 (200215) A61K031-4045
ZA 2001000607 A 20020925 (200275) 78p A61K000-00
HU 2001000321 A2 20021028 (200277) A61K031-404
ADT AU 2001016399 A AU 2001-16399 20010123; CA 2331847 A1 CA 2001-2331847 20010122; JP 2001206856 A JP 2001-14036 20010123; EP 1125580 A2 EP 2001-300575 20010123; US 2001046958 A1 Provisional US 2000-177770P 20000124, US 2001-767633 20010123; KR 2001083148 A KR 2001-3820 20010126; ZA 2001000607 A ZA 2001-607 20010122; HU 2001000321 A2 HU 2001-321 20010123
PRAI US 2000-177770P 20000124; US 2001-767633 20010123
IC ICM A61K000-00; A61K031-00; A61K031-404; A61K031-4045; A61K031-405; A61K045-00
ICS A61K031-407; A61K031-427; A61K031-44; A61K031-4439; A61K031-454; A61K031-496; A61K031-5355; A61K031-5377; A61K031-541; A61K031-695; A61K038-04; A61K038-28; A61K045-06; A61P003-00; **A61P003-04**; A61P003-06; A61P003-10; A61P005-00; A61P005-02; A61P005-14; A61P005-42; A61P005-48; A61P007-04; A61P009-00; A61P009-02; A61P009-04; A61P009-10; A61P009-12; A61P009-14; A61P011-00; A61P043-00
ICA C07D209-42; C07D401-12; C07D403-12
AB AU 200116399 A UPAB: 20011108
NOVELTY - Treating diabetic cardiomyopathy involves administering a glycogen phosphorylase inhibitor (A).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:
(1) a pharmaceutical composition comprising (A) and a carrier, excipient or adjuvant; and
(2) a kit comprising the pharmaceutical composition; and instructions for use.
ACTIVITY - Antidiabetic; Hypotensive; Cardiant; Anorectic; Antilipemic.
MECHANISM OF ACTION - alpha 2-antagonist; PPAR- gamma agonist; Fatty acid oxidation inhibitor; alpha -glucosidase inhibitor; beta -agonist; Phosphodiesterase inhibitor; amylin antagonist; glucagon antagonist; gluconeogenesis inhibitor; Aldose reductase inihbitor; Sorbitol dehydrogenase inhibitor; Glucocorticoil receptor antagonist, NHE-1 inhibitor.
USE - In the manufacture of a medicament for treating diabetic cardiomyopathy, diabetes, cardiovascular disease, ischemic heart disease, congestive heart failure; for treating a diabetic patient who is at a risk of suffering from myocardial ischemia and reperfusion; also for treating hypertension, diastolic blood pressure abnormalities, microvascular diabetic complications, abnormal left ventricular function, myocardial fibrosis, abnormal cardiac function, pulmonary congestion, small vessel disease, coagulopathy, cardiac contusion, myocardial infarction and small vessel disease without atherosclerotic cardiovascular disease or luminal narrowing (all claimed).
ADVANTAGE - (A) prevents the patients from undergoing balloon angioplasty, bypass surgery and major non-cardiac surgery.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-J03A; **B04-J10**; B05-A03B; B06-D01; B14-D03; B14-F01B; B14-F02; B14-F02B; B14-F04; B14-F09; B14-K01
TECH UPTX: 20011108
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: (A) also contains an addtional compound selected from insulin analogs, biguanide, alpha2-antagonist, imidazoline, glitazone, PPAR-gamma agonist, fatty acid oxidation inhibitor, alpha-glucosidase inhibitor, beta-agonist, phosphodiesterase inhibitor, lipid-lowering agent, **antiobesity** agent, vanadate, vanadium and peroxovanadium complex, amylin antagonist,

glucagon antagonist, gluconeogenesis inhibitor, somatostatin analog and antagonist or antilipolytic agent, aldose reductase inihbitor, sorbitol dehydrogenase inhibitor, glucocorticoil receptor antagonist, NHE-1 inhibitor or thyromimetic.

ABEX UPTX: 20011108

SPECIFIC COMPOUNDS - 5-Chloro-1H-indole-2-carboxylic acid ((1S)-((R)-hydroxy-dimethylcarbamoyl-methyl)-2-phenyl-ethyl)-amide; 5,6-dichloro-1H-indole-2-carboxylic acid ((1S)-((R)-hydroxy-(methoxy-methylcarbamoyl)-methyl)-2-phenyl-ethyl)-amide; 5-chloro-1H-indole-2-carboxylic acid ((1S)-((R)-hydroxy-(methoxy-methyl-carbamoyl)-methyl)-2-phenyl-ethyl)-amide; 5-chloro-1H-indole-2-carboxylic acid ((1S)-((R)-hydroxy-((2-hydroxy-ethyl)- methyl-carbamoyl)-methyl)-2-phenyl-ethyl)-amide; 5-chloro-1H-indole-2-carboxylic acid ((1S)-benzyl-3-((3R,4S)-dihydroxy-pyrrolidin-1-yl)-(2R)-hydroxy-3-oxo-propyl)-amide; 5-chloro-1H-indole-2-carboxylic acid ((1S)-((R)-hydroxy-(methyl-pyridin-2-yl-carbamoyl)-methyl)-2-phenyl-ethyl)-amide; and 5-chloro-1H-indole-2-carboxylic acid ((1S)-((R)-hydroxy-(methyl(2-pyridin-2-yl-ethyl)-carbamoyl)-methyl)-2-phenyl-ethyl)-amide are specifically claimed as (A).

ADMINISTRATION - (A) can be administered to a patient orally, rectally, parenterally (preferably intrevenously, intramuscularly or subcutneously), intracisternally, intravaginally, intraperitoneally, intravesically, locally or as a buccal or nasal spray.
(A) is administered to the patient in a dosage of about 0.7 - 7000 mg/day.
(A) is administered orally or parenterally to an animal in a daily dosage of about 0.01 - 100 (preferably 0.1 - 50) mg/kg.

EXAMPLE - No relevant example given.

L115 ANSWER 11 OF 15 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **2001-425859** [45] WPIX
DNC **C2001-128888**
TI Suppressing the appetite and reducing weight gain in animals, e.g., chickens, pigs and humans comprises administering an antibody to a gut peptide, e.g., cholecystokinin, bombesin or somatostatin.
DC B04 C06
IN COOK, M E; STRANSKY, D L; JEROME, D L
PA (WISC) WISCONSIN ALUMNI RES FOUND; (COOK-I) COOK M E; (STRA-I) STRANSKY D L
CYC 94
PI WO 2001051086 A1 20010719 (200145)* EN 15p A61K039-395
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001026355 A 20010724 (200166) A61K039-395
US 2002150575 A1 20021017 (200270) A61K039-395
ADT WO 2001051086 A1 WO 2001-US542 20010108; AU 2001026355 A AU 2001-26355 20010108; US 2002150575 A1 US 2000-479811 20000107
FDT AU 2001026355 A Based on WO 2001051086
PRAI US 2000-479811 20000107
IC ICM A61K039-395
ICS A61K039-40; A61K039-42
AB WO 200151086 A UPAB: 20010813
NOVELTY - Suppressing the appetite in an animal, comprising administering an antibody (I) to a gut peptide (II), is new.
ACTIVITY - Anorectic.
Anti-cholecystokinin (anti-CCK) antibodies were generated in eggs, titers were determined and diet/egg yolk mixtures containing the desired antibody dose were made.
Four groups of eight pigs were fed, for three weeks, with a control

diet, and a diet having anti-CCK antibody titer per kg of feed of 5936, 17808, and 59360, respectively. Diets having high anti-CCK antibody titer reduced weight gain in pigs which resulted in a net reduced weight gain after 3 weeks of feeding. No treatment resulted in gain (kg) of 6.36, compared to 5.91, 5.45, and 4.54 (kg) for the three antibody titers.

MECHANISM OF ACTION - Appetite suppressant; gut peptide antagonist/inhibitor; cholecystokinin/bombesin/somatostatin antagonist/inhibitor.

Pigs fed, for three weeks, with a control diet, and a diet having an anti-CCK antibody titer showed a reduction in food consumed in respect of increasing titers of the antibody. Compared to the control of 12.52 kg of food consumed, increasing titers gave consumption (kg) of 12.52, 11.61, and 11.51 for titers of 5936, 17808, and 59360, respectively.

USE - For suppressing appetite and reducing weight gain in animals, e.g., chickens, pigs and humans (claimed).

ADVANTAGE - Allows the control (increase or decrease) of food intake and weight gain as desired at various stages in an animal's life or development.

Dwg.0/2

FS CPI
FA AB; DCN
MC CPI: B04-G01; B04-J01; **B04-J10**; B04-J13; **B14-E12**;
C04-G01; C04-J01; **C04-J10**; C04-J13; **C14-E12**
TECH UPTX: 20010813

TECHNOLOGY FOCUS - BIOLOGY - Preferred Method: The method preferably comprises:

(1) immunizing a producer animal with a gut peptide (II) to produce and antibody (I) to (II);
(2) isolating a substance (III) containing (I); and
(3) feeding the (III) to an animal for a period of time.

(II) may be cholecystokinin, bombesin or somatostatin. The animal may be avian, preferably a chicken, or a mammal selected from porcine, bovine, ovine, caprine, rodent, swine, and human.

ABEX UPTX: 20010813

ADMINISTRATION - Administration is oral (feeding) (claimed). No dosage details given.

L115 ANSWER 12 OF 15 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-146787 [15] WPIX
DNC C2001-043352
TI New polypeptide compounds are somatostatin and neuromedin B receptor agonists, for treating a wide range of disorders e.g. cancer, gastrointestinal disorders and inflammatory disorders.
DC B04
IN MORGAN, B A; SADAT-AALAEE, D
PA (SCRC) SOC CONSEILS RECH & APPL SCI; (SCRC) SAS SOC CONSEILS RECH & APPL SCI; (SCRC) SCRAS SOC CONSEILS RECH & APPL SCI; (BIOM-N) BIOMEASURE INC
CYC 92
PI WO 2000075186 A1 20001214 (200115)* EN 85p C07K014-655
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000054633 A 20001228 (200119) C07K014-655
EP 1189941 A1 20020327 (200229) EN C07K014-655
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
BR 2000011680 A 20020430 (200237) C07K014-655
CZ 2001004297 A3 20020612 (200251) C07K014-655
HU 2002002022 A2 20021028 (200277) C07K014-655
CN 1367793 A 20020904 (200281) C07K014-655

JP 2003501443 W 20030114 (200306) 116p C07K007-06

ADT WO 2000075186 A1 WO 2000-US15396 20000605; AU 2000054633 A AU 2000-54633 20000605; EP 1189941 A1 EP 2000-939563 20000605, WO 2000-US15396 20000605; BR 2000011680 A BR 2000-11680 20000605, WO 2000-US15396 20000605; CZ 2001004297 A3 WO 2000-US15396 20000605, CZ 2001-4297 20000605; HU 2002002022 A2 WO 2000-US15396 20000605, HU 2002-2022 20000605; CN 1367793 A CN 2000-811215 20000605; JP 2003501443 W WO 2000-US15396 20000605, JP 2001-502467 20000605

FDT AU 2000054633 A Based on WO 2000075186; EP 1189941 A1 Based on WO 2000075186; BR 2000011680 A Based on WO 2000075186; CZ 2001004297 A3 Based on WO 2000075186; HU 2002002022 A2 Based on WO 2000075186; JP 2003501443 W Based on WO 2000075186

PRAI US 1999-137655P 19990604

IC ICM C07K007-06; C07K014-655

ICS A61K038-00; **A61K038-31**; A61P001-00; A61P001-02; A61P001-12; A61P001-18; A61P003-00; **A61P003-04**; A61P003-06; A61P005-10; A61P005-14; A61P005-18; A61P005-42; A61P005-48; A61P007-00; A61P009-00; A61P009-02; A61P009-10; A61P009-12; A61P013-12; A61P015-00; A61P017-00; A61P019-02; A61P019-08; A61P025-00; A61P025-18; A61P025-28; A61P025-36; A61P027-02; A61P031-04; A61P031-18; A61P035-00; A61P035-02; A61P037-06; A61P043-00; C07K014-47

AB WO 200075186 A UPAB: 20011129

NOVELTY - New polypeptide compounds (I) and their salts are new.

DETAILED DESCRIPTION - New polypeptide compounds of formula (I) and their salts are new. alpha -nitrogen of AA1 - AA8 = optionally substituted;

AA1 = absent or the D- or L- isomer of R11, Aac, Aic, Arg, Asn, Asp, Dip, Gln, Glu, Hca, Hyp, Lys, Mac, Macab, Orn, Pro, Ser, Ser(Bzl), Thr, Thr(Bzl), Pip, hArg, Bip, Bpa, Tic, Cmp, Inc, Inp, Nip, Ppc, Htic, Thi, Tra, Cmpi, Tpr, Iia, Alla, Aba, Gba, Car, Ipa, Iaa, Inip, Apa, Mim, Thnc, Sala, Aala, Thza, Thia, Bal, Fala, Pala, Dap, Agly, Pgly, Ina, Dipa, Mnf, Inic, C4c, 5-Iqs, Htqa, 4-Mqc, Thn, alpha -Chpa, Cit, Nua, Pyp or an aromatic alpha -amino acid (optionally substituted);

AA2 = absent or the D- or L- isomer of R11, Aic, Arg, Hca, His, Hyp, Pal, F5-Phe, Phe, Pro, Trp, X0-Phe Pip, hArg, Bip, Bpa, Tic, Cmp, Inc, Inp, Nip, Ppc, Htic, Thi, Tra, Cmpi, Tpr, Iia, Alla, Aba, Gba, Car, Ipa, Iaa, Inip, Apa, Mim, Thnc, Sala, Aala, Thza, Thia, Bal, Fala, Pala, Dap, Agly, Pgly, Ina, Dipa, Mnf, Inic, 1-Iqc, 3-Iqc, C4c, 5-Iqs, Htqa, 4-Mqc, Thn, alpha -Chpa, Cit, Nua, or Pyp;

AA3 = absent or the D- or L- isomer of Cys, hCys, Pen, Tpa, Tmpa, Mac, Macab or an aromatic alpha -amino acid (optionally substituted);

AA3b = absent or the D- or L- isomer of Pal, 4-Pal, His, Arg, Nal, Trp, Bpa, F5-Phe, Phe, X0-Phe, R11, hArg, Bip, Tic, Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala or Pala;

AA4 = D- or L- isomer of Trp, Lys, Orn, hLys, cis-4-Acha, trans-4-Acha, trans-4-Amcha, 4-Pip-Gly, N-Met-Trp, beta -Met-Trp, His, hHis, hArg, Bip, Tic, Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala or 4-Pip-Ala (optionally substituted), or an aromatic alpha -amino acid (optionally substituted);

AA5 = absent, R11, Aic, A3c, A4c, A5c, A6c, Abu, Aib, beta -Ala, Bpa, Cha, Deg, Gaba, Ile, Leu, Nal, Nle, Pro, Ser, Sar, Ser(Bzl), Thr, Thr(Bzl), Trp, Val, Pal, F5Phe, Phe, X0-Phe, or the D- or L- isomer of 4-Pip-Gly, 4-Pip-Ala, cis-4-Acha, trans-4-Acha, trans-4-Amcha, hLys, Lys, Orn, hArg, Bip, Tic, Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala or Pala (optionally substituted);

AA6 = absent or the D- or L-isomer of R11, optionally substituted aromatic alpha --amino acid, Cys, hCys, Pen, Tpa, Tmpa, Thr, Thr(Bzl), Ser, Ser(Bzl), hArg, Bip, Tic, Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala or Pala;

AA7 = absent or the D- or L-isomer of R11, optionally substituted aromatic alpha -amino acid, A3c, A4c, A5c, A6c, Abu, Aib, Aic, beta -Ala, Arg, Cha, Deg, Gaba, Ile, Leu, Nle, Pip, Pro, Sar, Ser, Ser(Bzl), Thr,

Thr(Bzl), Val, Tic, Htic, Sala, Aala, Thza, Thia, Bal, Fala, Pala, hArg, Bip, Bpa, Dip, Pal, Sala or X0-Phe;

AA7b = absent or the D- or L-isomer of R11, Bpa, Phe, F5-Phe, Phe, X0-Phe, Nal, Pro, Ser, Ser(Bzl), Thr, Thr(Bzl), Trp, hArg, Bip, Tic, Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, Pala or Bpa;

AA8 = absent or the D- or L-isomer of R11, Maa, Maaab, Thr, Thr(Bzl), Ser, Ser(Bzl), tyr, Phe(4-O-Bzl), F5-Phe or X0-Phe, or an optionally substituted aromatic alpha -amino acid;

R1, R2 = H, E, E(O)2S-, E(O)C-, EOOC-, R13 or absent;

R5 = OR6, NR7R8 or absent;

R6 - R8 = 1-12C alkyl, 2-12C alkenyl, 2-12C alkynyl, phenyl, naphthyl, phenyl-1-6C alkyl, phenyl-2-6C alkenyl, phenyl-2-6C alkynyl, naphthyl-1-6C alkyl, naphthyl-2-6C alkenyl, naphthyl-2-6C alkynyl, 1-adamantyl, 2-adamantyl, 9-fluorenylmethyl, dicyclopropylmethyl, dimethylcyclopropylmethyl or benzhydryl;

R9, R10 = H, 1-6C alkyl, 3-4C alkenyl, 3-4C alkynyl, 1-adamantyl or 2-adamantyl;

R11 = a group of formula (i)-(vi);

n = 1-3;

p = 0-2;

R12 = a group of formula (vii)-(x) (all optionally substituted);

R13 = a group of formula (xi);

q, r, s, t = 0-5;

R19 = absent, H, NH2, OH, 1-6C hydroxyalkyl, N(R27R28), SO3H, or phenyl, naphthyl or heterocyclyl (all optionally substituted);

R20 = O or absent;

R21, R23 = 1-6C alkyl or absent;

R22 = N, O, C or CH;

R24 = N, C or CH;

R25 = NH, O or absent;

R26 = SO2, CO or CH;

R27, R28 = H or 1-6C alkyl;

E = R3 (optionally substituted);

X0 = halo, nitro, OH, 1-6C alkyl, 1-6C alkoxy, mono- or dialkylamino, CN, Bzl or O-Bzl;

X1 = H, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, indolyl, imidazolyl, 1-naphthyl, 3-pyridyl, a moiety corresponding to the sidechain group of Ala, Lys, His, Arg, Leu, Gln, Tyr, Thr, Trp, Phe or Val, or benzyl (optionally ring substituted);

X2, X3 = H, halo, OH, =O, =S, 1-12C alkyl, 2-12C alkenyl, 2-12C alkynyl, phenyl, naphthyl, phenyl-1-6C alkyl, phenyl-2-6C alkenyl, phenyl-2-6C alkynyl, naphthyl-1-6C alkyl, naphthyl-2-6C alkenyl, naphthyl-2-6C alkynyl, 3-7C cycloalkyl-1-6C alkyl, 3-7C cycloalkyl-2-6C alkenyl, 3-7C cycloalkyl-2-6C alkynyl, heterocyclyl-1-6C alkyl, heterocyclyl-2-6C alkenyl, heterocyclyl-2-6C alkynyl, 1-adamantyl, 2-adamantyl, dicyclopropylmethyl or dimethylcyclopropylmethyl;

X4 = H, OH or NH2; and

X5 = halo, NO2, Me, OH, Bzl or O-Bzl;

with provisos given in Definitions section.

ACTIVITY - Cytostatic; anabolic; antithyroid; antiproliferative; cardiant; antiinflammatory; antidiabetic; gastrointestinal; antiulcer; antidiarrheal; anti-HIV; neuroprotective; gynecological; osteopathic; hepatotropic; hypertensive; hypotensive; tranquilizer; antilipemic; nephrotropic; antiarthritic; immunosuppressive; anorectic; antiaddictive.

MECHANISM OF ACTION - Neuromedin B and Somatostatin receptor agonist.

Details of assays for binding of (I) to somatostatin subtype receptors was determined by measuring inhibition of (125I-Tyr11)SRIF-14 binding to CHO-K1 cells transfected with the sst receptor subtype. No biological data given.

USE - (I) are useful for eliciting a neuromedin B and/or somatostatin receptor agonist effect (especially SSTR-1) for treatment of lung cancer, glioma, anorexia, hypothyroidism, hypoaldosteronism, H. pylori proliferation, acromegaly, restenosis, Crohn's disease, systemic

sclerosis, external and internal pancreatic pseudocysts and ascites, VIPoma, nesidoblastosis, hyperinsulinism, gastrinoma, Zollinger-Ellison syndrome, diarrhea, AIDS related diarrhea, chemotherapy related diarrhea, scleroderma, irritable bowel syndrome, pancreatitis, small bowel obstruction, gastroesophageal reflux, duodenogastric reflux, Cushing's syndrome, gonadotropinoma, hyperparathyroidism, Graves' disease, diabetic neuropathy, Paget's disease, polycystic ovary disease, thyroid cancer, hepatome, leukemia, meningioma, cancer cachexia, orthostatic hypotension, postprandial hypotension, panic attacks, GH secreting adenomas, insulinoma, glucagonoma, diabetes mellitus, hyperlipidemia, insulin insensitivity, Syndrome X, angiopathy, proliferative retinopathy, dawn phenomenon, nephropathy, gastric acid secretion, peptic ulcers, enterocutanous fistula, pancreaticocutaneous fistula, Dumping syndrome, watery diarrhea syndrome, pancreatitis, gastrointestinal hormone secreting tumor, angiogenesis, arthritis, allograft rejection, graft vessel bleeding, portal hypertension, gastrointestinal bleeding, obesity and opioid overdose (all claimed).

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B04-C01A; B04-C01B; B14-A01; B14-C09; B14-D01E; B14-E01; B14-E08; B14-E10; B14-E11; **B14-E12**; B14-F02; B14-F06; B14-F08; B14-H01; B14-J01B4; B14-M01C; B14-N03; B14-N10; B14-N11; B14-N13; B14-S01

TECH UPTX: 20010317

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: The polypeptides are made by solid phase combinatorial synthesis on Rink Amide MBHA resin with FMOC protecting group protocol, and cleaved with a trifluoroacetic acid/phenol/water/triisopropylsilane (83 ml/5 g/10 ml/2 ml) mixture.

ABEX UPTX: 20010317

SPECIFIC COMPOUNDS - 175 Compounds (I) are specifically claimed e.g. Ac-D-Phe-Tyr-cyclo-(D-Cys-D-Trp-Lys-Cys)-Abu-Thr-NH2 (Ia).

ADMINISTRATION - Administration is 0.0001-100, preferably 0.01-10 mg/kg/day e.g. orally, parenterally, nasally, vaginally, rectally, sublingually or topically.

EXAMPLE - Rink Amide MBHA resin (1 g) was placed in a preprogrammed Model 90 peptide synthesizer. The resin was stirred with FMOC-Nal (2.12 mmol), 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (2.01 mmol) and diisopropyl ethylamine (4.24 mmol) in dimethylformamide (DMF) for 90 minutes, and the resulting amino acid resin was cycled through the synthesis program. The Nal-resin was coupled with Fmoc-Abu, then cycled again, and dried under vacuum. Fmoc-S-trityl-D-Cys, Fmoc-N-epsilon-t-Boc-Lys and Fmoc-N-in-t-Boc-Trp (1.4 mmol) were successively coupled to the peptide resin (0.35 mmol). After drying, the peptide resin was split and one portion coupled with Fmoc-S-trityl-D-Cys, Fmoc-O-t-butyl-Tyr. The coupled portion was split again and one portion coupled with Fmoc-Nal. After washing with DMF and drying, the complete resin weighted 0.242 g. this resin was mixed with trifluoroacetic acid/phenol/water/triisopropylsilane (8.8 ml/0.5 g/0.5 ml/0.2 ml) mixture and stirred for 150 minutes. Excess trifluoroacetic acid was removed under reduced pressure to give an oily residue. Ether was added to precipitate the free peptide. The crude peptide was dissolved in 11 ml acetonitrile/water/0.1 N acetic acid (5/5/1 ml), followed by addition of 200 mg EKATHIOX (RTM) resin. The mixture was stirred overnight and filtered. The filtrate was evaporated to small volume and purified by HPLC to give H-Nal-Tyr-D-Cys-D-Trp-Lys-D-Cys-Abu-Nal-NH2 (I').

DEFINITIONS - New polypeptide compounds of formula (I) and their salts are new.

alpha-nitrogen of AA1 - AA8 = optionally substituted by 1-4C alkyl, 3-4C alkenyl, 3-4C alkynyl or 1-6C alkyl-C(O)-;

AA1 = absent or the D- or L- isomer of R11, Aac, Aic, Arg, Asn, Asp, Dip,

Gln, Glu, Hca, Hyp, Lys, Mac, Macab, Orn, Pro, Ser, Ser(Bzl), Thr, Thr(Bzl), Pip, hArg, Bip, Bpa, Tic, Cmp, Inc, Inp, Nip, Ppc, Htic, Thi, Tra, Cmpi, Tpr, Iia, Alla, Aba, Gba, Car, Ipa, Iaa, Inip, Apa, Mim, Thnc, Sala, Aala, Thza, Thia, Bal, Fala, Pala, Dap, Agly, Pgly, Ina, Dipa, Mnf, Inic, C4c, 5-Iqs, Htqa, 4-Mqc, Thn, alpha-Chpa, Cit, Nua, Pyp or an aromatic alpha-amino acid (optionally substituted by X);
X = halo, nitro, OH, CN, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 1-6C alkoxy, Bzl, O-Bzl or NR9R10;
AA2 = absent or the D- or L- isomer of R11, Aic, Arg, Hca, His, Hyp, Pal, F5-Phe, Phe, Pro, Trp, X0-Phe Pip, hArg, Bip, Bpa, Tic, Cmp, Inc, Inp, Nip, Ppc, Htic, Thi, Tra, Cmpi, Tpr, Iia, Alla, Aba, Gba, Car, Ipa, Iaa, Inip, Apa, Mim, Thnc, Sala, Aala, Thza, Thia, Bal, Fala, Pala, Dap, Agly, Pgly, Ina, Dipa, Mnf, Inic, 1-Iqc, 3-Iqc, C4c, 5-Iqs, Htqa, 4-Mqc, Thn, alpha-Chpa, Cit, Nua, or Pyp;
AA3 = absent or the D- or L- isomer of Cys, hCys, Pen, Tpa, Tmpa, Mac, Macab or an aromatic alpha-amino acid (optionally substituted by Y);
Y = halo, nitro, OH, CN, 1-4C alkyl, 2-4C alkenyl, 2-4C alkynyl, 1-4C alkoxy, Bzl, O-Bzl, NR9R10, Pip, hArg, Bip, Bpa, Tic, Cmp, Inc, Inp, Nip, Ppc, Htic, Thi, Tra, Cmpi, Tpr, Iia, Alla, Aba, Gba, Car, Ipa, Iaa, Inip, Apa, Mim, Thnc, Sala, Aala, Thza, Thia, Bal, Fala, Pala, Dap, Agly, Pgly, Ina, Dipa, Mnf, Inic, 1-Iqc, 3-Iqc, C4c, 5-Iqs, Htqa, 4Mqc, Thn, alpha-Chpa, Cit, Nua or Pyp;
AA3b = absent or the D- or L- isomer of Pal, 4-Pal, His, Arg, Nal, Trp, Bpa, F5-Phe, Phe, X0-Phe, R11, hArg, Bip, Tic, Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala or Pala;
AA4 = D- or L- isomer of Trp, Lys, Orn, hLys, cis-4-Acha, trans-4-Acha, trans-4-Amcha, 4-Pip-Gly, N-Met-Trp, beta-Met-Trp, His, hHis, hArg, Bip, Tic, Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala or 4-Pip-Ala (optionally substituted by R3 and R4), or an aromatic alpha-amino acid (optionally substituted by Z);
Z = halo, nitro, OH, CN, 1-4C alkyl, 2-4C alkenyl, 2-4C alkynyl, 1-4C alkoxy, Bzl, O-Bzl or NR9R10;
AA5 = absent, R11, Aic, A3c, A4c, A5c, A6c, Abu, Aib, beta-Ala, Bpa, Cha, Deg, Gaba, Ile, Leu, Nal, Nle, Pro, Ser, Sar, Ser(Bzl), Thr, Thr(Bzl), Trp, Val, Pal, F5Phe, Phe, X0-Phe, or the D- or L- isomer of 4-Pip-Gly, 4-Pip-Ala, cis-4-Acha, trans-4-Acha, trans-4-Amcha, hLys, Lys, Orn, hArg, Bip, Tic, Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala or Pala (optionally substituted by R3 and R4);
AA6 = absent or the D- or L-isomer of R11, optionally substituted aromatic alpha--amino acid, Cys, hCys, Pen, Tpa, Tmpa, Thr, Thr(Bzl), Ser, Ser(Bzl), hArg, Bip, Tic, Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala or Pala;
AA7 = absent or the D- or L-isomer of R11, optionally substituted aromatic alpha-amino acid, A3c, A4c, A5c, A6c, Abu, Aib, Aic, beta-Ala, Arg, Cha, Deg, Gaba, Ile, Leu, Nle, Pip, Pro, Sar, Ser, Ser(Bzl), Thr, Thr(Bzl), Val, Tic, Htic, Sala, Aala, Thza, Thia, Bal, Fala, Pala, hArg, Bip, Bpa, Dip, Pal, Sala or X0-Phe;
AA7b = absent or the D- or L-isomer of R11, Bpa, Phe, F5-Phe, Phe, X0-Phe, Nal, Pro, Ser, Ser(Bzl), Thr, Thr(Bzl), Trp, hArg, Bip, Tic, Htic, Dip, Sala, Aala, Thza, Thia, Bal, Fala, Pala or Bpa;
AA8 = absent or the D- or L-isomer of R11, Maa, Maaab, Thr, Thr(Bzl), Ser, Ser(Bzl), tyr, Phe(4-O-Bzl), F5-Phe or X0-Phe, or an optionally substituted aromatic alpha-amino acid;
R1, R2 = H, E, E(O)2S-, E(O)C-, EOOC-, R13 or absent;
R3, R4 = 1-12C alkyl, 2-12C alkenyl, 2-12C alkynyl, phenyl, naphthyl, phenyl-1-6C alkyl, phenyl-2-6C alkenyl, phenyl-2-6C alkynyl, naphthyl-1-6C alkyl, naphthyl-2-6C alkenyl, naphthyl-2-6C alkynyl, 3-7C cycloalkyl-1-6C alkyl, 3-7C cycloalkyl-2-6C alkenyl, 3-7C cycloalkyl-2-6C alkynyl, heterocyclyl-1-4C alkyl, heterocyclyl-2-4C alkenyl, heterocyclyl-2-4C alkynyl, 1-adamantyl, 2-adamantyl, 9-fluorenylmethyl, dicyclopropylmethyl, dimethylcyclopropylmethyl or benzhydryl;
R5 = OR6, NR7R8 or absent;
R6 - R8 = 1-12C alkyl, 2-12C alkenyl, 2-12C alkynyl, phenyl, naphthyl,

phenyl-1-6C alkyl, phenyl-2-6C alkenyl, phenyl-2-6C alkynyl, naphthyl-1-6C alkyl, naphthyl-2-6C alkenyl, naphthyl-2-6C alkynyl, 1-adamantyl, 2-adamantyl, 9-fluorenylmethyl, dicyclopropylmethyl, dimethylcyclopropylmethyl or benzhydryl;
R9, R10 = H, 1-6C alkyl, 3-4C alkenyl, 3-4C alkynyl, 1-adamantyl or 2-adamantyl;
R11 = a group of formula (i)-(vi);
n = 1-3;
p = 0-2;
R12 = a group of formula (vii)-(x) (all optionally substituted);
R13 = a group of formula (xi);
q, r, s, t = 0-5;
R19 = absent, H, NH2, OH, 1-6C hydroxyalkyl, N(R27R28), SO3H, or phenyl, naphthyl or heterocyclyl (all optionally substituted by halo, nitro, OH, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 1-6C alkoxy, NH2, mono- or dialkylamino, Bzl or O-Bzl);
R20 = O or absent;
R21, R23 = 1-6C alkyl or absent;
R22 = N, O, C or CH;
R24 = N, C or CH;
R25 = NH, O or absent;
R26 = SO2, CO or CH;
R27, R28 = H or 1-6C alkyl;
E = R3 (optionally substituted by halo, Bzl, OH, O-Bzl, CN, NO2, COOH or SH);
X0 = halo, nitro, OH, 1-6C alkyl, 1-6C alkoxy, mono- or dialkylamino, CN, Bzl or O-Bzl;
X1 = H, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, indolyl, imidazolyl, 1-naphthyl, 3-pyridyl, a moiety corresponding to the sidechain group of Ala, Lys, His, Arg, Leu, Gln, Tyr, Thr, Trp, Phe or Val, or benzyl (optionally ring substituted by halo, OH, 1-6C alkoxy, mono- or di-1-6C alkylamino, 1-4 alkyl, 2-4C alkenyl, 2-4C alkynyl, or NR9R10);
X2, X3 = H, halo, OH, =O, =S, 1-12C alkyl, 2-12C alkenyl, 2-12C alkynyl, phenyl, naphthyl, phenyl-1-6C alkyl, phenyl-2-6C alkenyl, phenyl-2-6C alkynyl, naphthyl-1-6C alkyl, naphthyl-2-6C alkenyl, naphthyl-2-6C alkynyl, 3-7C cycloalkyl-1-6C alkyl, 3-7C cycloalkyl-2-6C alkenyl, 3-7C cycloalkyl-2-6C alkynyl, heterocyclyl-1-6C alkyl, heterocyclyl-2-6C alkenyl, heterocyclyl-2-6C alkynyl, 1-adamantyl, 2-adamantyl, dicyclopropylmethyl or dimethylcyclopropylmethyl;
X4 = H, OH or NH2; and
X5 = halo, NO2, Me, OH, Bzl or O-Bzl;
provided that: (a) at least 6 amino acids are present; (b) when AA3 is Cys, hCys, Pen, Tpa or Tmpa, AA3 and AA6 are connected by a disulfide bond; (c) when AA1 or AA3 is mac or Macab, AA1 or AA3 is connected to AA8 by a disulfide bond; (d) AA2 can only be Hca when AA1 is absent; (e) when one of R1 or R2 is E(O)2S, E(O)C, EOOC or R13, then the other is H; (f) when R5 is absent, one of R1 or R2 is absent, and the N-terminal amino acid and C-terminal amino acid together form an amide bond; (g) when one of X2 or X3 is C=O or C=S, the other is absent; and (h) (I) is not D-Phe-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr-NH2, Ac-Phe-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr-NH2, L-4-NO2-Phe-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr-NH2, Ac-L-4-NO2-Phe-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr-NH2, Hca-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Abu-Thr-NH2, D-Dip-Tyr-cyclo(D-Cys-D-Trp-Lys-Cys)-Val-Tyr-NH2, D-4-NO2-Phe-Phe-(4-O-Bzl)-cyclo(D-Cys-D-Trp-Lys-Cys)-Cha-Nal-NH2 or D-4-NO2-Phe-cyclo-(D-Cys-Phe-(4-O-Bzl)-D-Trp-Lys-Cys)-Val-Tyr-NH2.

L115 ANSWER 13 OF 15 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-059686 [05] WPIX
DNC C1999-017523
TI Treating insulin resistance and syndrome X by administration of somatostatin or its agonist - for treating **obese** patients and to restore or maintain insulin sensitivity.

DC B04
IN CAWTHORNE, M A; LIU, Y; SENNITT, M V
PA (SCRC) SCRAS SOC CONSEILS RECH & APPL SCI
CYC 83
PI WO 9851332 A1 19981119 (199905)* EN 54p A61K038-31 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9880198 A 19981208 (199916) A61K038-31 <--
EP 980253 A1 20000223 (200015) EN A61K038-31 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9851332 A1 WO 1998-EP3000 19980513; AU 9880198 A AU 1998-80198 19980513; EP 980253 A1 EP 1998-928308 19980513, WO 1998-EP3000 19980513
FDT AU 9880198 A Based on WO 9851332; EP 980253 A1 Based on WO 9851332
PRAI US 1997-854943 19970513
IC ICM **A61K038-31**
AB WO 9851332 A UPAB: 19990203
Insulin resistance and/or syndrome X are treated by administration of somatostatin (I) or its agonists (II).
USE - The method is especially used to treat **obese** subjects, to restore or maintain insulin sensitivity, or (in syndrome X patients) to reduce plasma lipid levels and blood pressure, and to alter body fat distribution, in both humans and animals.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-C01; **B04-J10**; **B14-E12**

L115 ANSWER 14 OF 15 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-059685 [05] WPIX
DNC C1999-017522
TI Reducing body weight by administration of somatostatin or its agonist - for treating **obese** patients or non-insulin-dependent diabetics.
DC B04
IN CAWTHORNE, M A; LIU, Y; SENNITT, M V
PA (SCRC) SCRAS SOC CONSEILS RECH & APPL SCI
CYC 83
PI WO 9851331 A1 19981119 (199905)* EN 40p A61K038-31 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9876550 A 19981208 (199916) A61K038-31 <--
EP 981363 A1 20000301 (200016) EN A61K038-31 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
EP 981363 B1 20030730 (200356) EN A61K038-31 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
DE 69816808 E 20030904 (200366) A61K038-31 <--
ADT WO 9851331 A1 **WO 1998-EP2999 19980513**; AU 9876550 A AU 1998-76550 19980513; EP 981363 A1 EP 1998-924317 19980513, **WO 1998-EP2999 19980513**; EP 981363 B1 EP 1998-924317 19980513, **WO 1998-EP2999 19980513**; DE 69816808 E DE 1998-616808 19980513, EP 1998-924317 19980513, **WO 1998-EP2999 19980513**
FDT AU 9876550 A Based on WO 9851331; EP 981363 A1 Based on WO 9851331; EP 981363 B1 Based on WO 9851331; DE 69816808 E Based on EP 981363, Based on WO 9851331
PRAI US 1997-854941 19970513
IC ICM **A61K038-31**

ICS A61K007-00; A61K007-48
AB WO 9851331 A UPAB: 19990203
Body weight is decreased by administration of somatostatin (I) or its agonists (II).
USE - The method is especially used to treat **obese** subjects or patients with non-insulin dependent diabetes, for therapeutic or cosmetic reasons, both humans and animals.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-C01B; B04-C01C; **B04-J10**; B04-N04A; B14-D01E; **B14-E12**

L115 ANSWER 15 OF 15 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1998-271636 [24] WPIX
DNC C1998-084636
TI Composition for treatment of the risk factors of syndrome X of Reaven - (hyperinsulinaemia syndrome) comprises somatostatin, diazoxide, cyclothiazide (or their analogues) and/or metformin.
DC B04
IN COHEN, Y
PA (COHE-I) COHEN Y
CYC 79
PI WO 9810786 A2 19980319 (199824)* EN 45p A61K038-31 <--
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9741339 A 19980402 (199833) A61K038-31 <--
ADT WO 9810786 A2 WO 1997-IL301 19970910; AU 9741339 A AU 1997-41339 19970910
FDT AU 9741339 A Based on WO 9810786
PRAI IL 1996-119403 19961010; IL 1996-119250 19960912
IC ICM **A61K038-31**
ICS A61K031-155; A61K031-54
AB WO 9810786 A UPAB: 19980617
Pharmaceutical composition, for treatment of the risk factors of syndrome X of Reaven (hyperinsulinaemia syndrome) comprises somatostatin, diazoxide, cyclothiazide (or an analogue of one of these) or metformin as the active ingredient.
USE - The composition reduces resistance to insulin, and so treats and prevents all the associated risk factors at once. The risk factors are hypertension, dyslipidaemia (raised triglyceride and LDL levels with reduced HDL levels), shorter coagulation time due to increased Plasminogen Activator Inhibitor-1 levels, core **obesity**, glucose intolerance hyperinsulinaemia. The composition reduces the incidence of ischaemic heart disease, cerebrovascular disorders, intermittent claudication, ischaemic bowel disease, impotence due to peripheral vascular disease, hypercoagulation (e.g. renal vein thrombosis), **obesity** and glucose intolerance.
Dosage is up to 8 mg/kg/day (calculated on diazoxide) in adults, and up to 15 mg/day in children, or up to 50 mu g/kg/day (calculated on octreotide), or up to 2.5g/day in 2-3 doses as metformin.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: **B04-J10**; B06-F03; B10-A17; B14-D02B; B14-E10C; **B14-E12**; B14-F01E; B14-F02B; B14-F04; B14-F06; B14-P02

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FILE 'DPCI' ENTERED AT 08:49:39 ON 11 FEB 2004

FILE LAST UPDATED: 4 FEB 2004 <20040204/UP>
PATENTS CITATION INDEX, COVERS 1973 TO DATE

>>> LEARNING FILE LDPCI AVAILABLE <<<

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L116 ANSWER 1 OF 1 DPCI COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-059685 [05] DPCI
DNC C1999-017522
TI Reducing body weight by administration of somatostatin or its agonist - for treating obese patients or non-insulin-dependent diabetics.
DC B04
IN CAWTHORNE, M A; LIU, Y; SENNITT, M V
PA (SCRC) SCRAS SOC CONSEILS RECH & APPL SCI
CYC 83
PI WO 9851331 A1 19981119 (199905)* EN 40p A61K038-31 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9876550 A 19981208 (199916) A61K038-31
EP 981363 A1 20000301 (200016) EN A61K038-31
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
EP 981363 B1 20030730 (200356) EN A61K038-31
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
DE 69816808 E 20030904 (200366) A61K038-31
ADT WO 9851331 A1 WO 1998-EP2999 19980513; AU 9876550 A AU 1998-76550 19980513; EP 981363 A1 EP 1998-924317 19980513, WO 1998-EP2999 19980513; EP 981363 B1 EP 1998-924317 19980513, WO 1998-EP2999 19980513; DE 69816808 E DE 1998-616808 19980513, EP 1998-924317 19980513, WO 1998-EP2999 19980513
FDT AU 9876550 A Based on WO 9851331; EP 981363 A1 Based on WO 9851331; EP 981363 B1 Based on WO 9851331; DE 69816808 E Based on EP 981363, Based on WO 9851331
PRAI US 1997-854941 19970513
IC ICM A61K038-31
ICS A61K007-00; A61K007-48
FS CPI

EXF EXAMINER'S FIELD OF SEARCH UPE: 20031116

IC EP 981363 B1 20030730
A61K038-31

CTCS CITATION COUNTERS

PNC.DI	0	Cited Patents Count (by inventor)
PNC.DX	5	Cited Patents Count (by examiner)
IAC.DI	0	Cited Issuing Authority Count (by inventor)
IAC.DX	2	Cited Issuing Authority Count (by examiner)
PNC.GI	0	Citing Patents Count (by inventor)
PNC.GX	0	Citing Patents Count (by examiner)
IAC.GI	0	Citing Issuing Authority Count (by inventor)
IAC.GX	0	Citing Issuing Authority Count (by examiner)

CRC.I 0 Cited Literature References Count (by inventor)
CRC.X 7 Cited Literature References Count (by examiner)

CDP CITED PATENTS UPD: 20031116

Cited by Examiner

CITING PATENT	CAT	CITED PATENT	ACCNO
EP 981363	A	No Citations	
EP 981363	B1	EP 657174	A 1995-208279/28
	PA:	(MAYO-N) MAYO FOUNDATION; (MAYO-N) MAYO FOUND MEDICAL RES & EDUCATION	
	IN:	LARUSSO, N F	
		WO 9635950	A 1997-011729/01
	PA:	(UYBU-N) UNIV BUCKINGHAM; (CAWT-I) CAWTHORNE M A; (DAVE-I) DAVENPORT M; (DUNM-I) DUNMORE S J; (BIOM-N) BIOMEASURE INC	
	IN:	CAWTHORNE, M A; DAVENPORT, M; DUNMORE, S J	
		WO 9711962	A 1997-212847/19
	PA:	(TULA) TULANE EDUCATIONAL FUND & BIOMEASURE INC; (BIOM-N) BIOMEASURE INC; (TULA) TULANE EDUCATIONAL FUND; (TULA) UNIV TULANE MEDICAL CENT	
	IN:	COY, D H; TAYLOR, J E; TAYLER, J E	
		WO 9809991	A 1998-193554/17
	PA:	(UNIW) UNIV WASHINGTON; (ZYMO) ZYMOGENETICS INC	
	IN:	BASKIN, D G; DALESSIO, D A; ENSINCK, J W; FRANCIS, B H; HOFFMAN, R C; LASCHANSKY, E C; VOGEL, R E; D'ALESSIO, D A	
		WO 9810786	A 1998-271636/24
	PA:	(COHE-I) COHEN Y	
	IN:	COHEN, Y	
WO 9851331	A X	EP 657174	A 1995-208279/28
	PA:	(MAYO-N) MAYO FOUNDATION; (MAYO-N) MAYO FOUND MEDICAL RES & EDUCATION	
	IN:	LARUSSO, N F	
	X	WO 9635950	A 1997-011729/01
	PA:	(UYBU-N) UNIV BUCKINGHAM; (BIOM-N) BIOMEASURE INC	
	IN:	CAWTHORNE, M A; DAVENPORT, M; DUNMORE, S J	
	X	WO 9711962	A 1997-212847/19
	PA:	(BIOM-N) BIOMEASURE INC; (TULA) TULANE EDUCATIONAL FUND	
	IN:	COY, D H; TAYLOR, J E; TAYLER, J E	
		WO 9809991	A 1998-193554/17
	PA:	(UNIW) UNIV WASHINGTON; (ZYMO) ZYMOGENETICS INC	
	IN:	BASKIN, D G; DALESSIO, D A; ENSINCK, J W; FRANCIS, B H; HOFFMAN, R C; LASCHANSKY, E C; VOGEL, R E	
		WO 9810786	A 1998-271636/24
	PA:	(COHE-I) COHEN Y	
	IN:	COHEN, Y	

REN LITERATURE CITATIONS UPR: 20031202

Citations by Examiner

CITING PATENT	CAT	CITED LITERATURE
EP 981363	B1	H-J S Huang et al, Supplement to Hypertension, Vol. 19, No. 1, 01.01.1992, pp I-101 to I-109

EP 981363	A	See references of WO 9851331A1
EP 981363	B1	CARRETTA R ET AL: "REDUCTION OF BLOOD PRESSURE IN OBESE HYPERINSULINAEMIC HYPERTENSIVE PATIENTS DURING SOMATOSTATIN INFUSION" JOURNAL OF HYPERTENSION, vol. 7, no. SUPPL. 06, 18 June 1989, page S196/S197 XP002053034
EP 981363	A	H-J S Huang et al, Supplement to Hypertension, Vol. 19, No. 1, 01.01.1992, pp I-101 to I-109
EP 981363	A	See also references of WO 9851331A1
WO 9851331	A	See also references of EP 0981363A1
WO 9851331	A	CARRETTA R ET AL: "REDUCTION OF BLOOD PRESSURE IN OBESE HYPERINSULINAEMIC HYPERTENSIVE PATIENTS DURING SOMATOSTATIN INFUSION" JOURNAL OF HYPERTENSION, vol. 7, no. SUPPL. 06, 18 June 1989, page S196/S197 XP002053034

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     (FILE 'HOME' ENTERED AT 07:39:34 ON 11 FEB 2004)
               SET COST OFF

     FILE 'HCAPLUS' ENTERED AT 07:39:44 ON 11 FEB 2004
L1             1 S WO98-EP2999/AP,PRN
               SEL RN

     FILE 'REGISTRY' ENTERED AT 07:40:01 ON 11 FEB 2004
L2           118 S E1-E118
L3            15 S L2 AND C6-C6/ES
L4            13 S L3 AND S/ELS
L5            11 S L4 AND 8/SQL
L6             4 S L5 NOT PHENYLALAN?
               SEL RN 4
L7             1 S E119

     FILE 'HCAPLUS' ENTERED AT 07:48:50 ON 11 FEB 2004
L8           320 S L7
L9           390 S ANGIOPEPTIN# OR ANGIO PEPTIN# OR BIM23014 OR BIM()(23014 OR 2
L10          417 S L8,L9
               E CAWTHORNE M/AU
L11          140 S E3-E7
               E LIU Y/AU
L12         1646 S E3,E21
               E LIU YONG/AU
L13          787 S E3,E41,E42
               E LIU YONGL/AU
L14           13 S E10,E11
               E SENNITT M/AU
L15           31 S E4-E6
               E SENNIT M/AU
               E SENIT M/AU
L16            4 S L10 AND L11-L15
L17          181 S L10 AND (PY<=1997 OR PRY<=1997 OR AY<=1997)
               E BODY WEIGHT/CT
L18        15919 S E3-E5
               E E3+ALL
L19        15919 S E2
               E E8+ALL
L20        18476 S E2+NT
               E E7+ALL
L21         4293 S E4,E3+NT
               E E8+ALL
L22         2009 S E4,E3+NT
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                E E10+ALL
L23         14601 S E2+NT
                E E7+ALL
L24           422 S E3+NT
                E OBESITY/CT
L25         18159 S E3-E7
                E E3+ALL
                E E6+ALL
L26         37600 S E4+NT
                E E13+ALL
                E E11+ALL
L27         29514 S E1
                E E6+ALL
L28          4622 S E3,E2
L29             2 S L17 AND L18-L28
L30             8 S L10 AND L18-L28
L31            10 S L16,L29-L30
L32             2 S L17 AND BODY()(WEIGHT OR WT OR MASS)
L33             0 S L17 AND BODY()FAT
L34             2 S L17 AND (WEIGHT OR WT)(L)(GAIN? OR LOSS OR LOSE OR LOSING)
L35             4 S L17 AND (WEIGHT OR WT)(L)REDUC?
L36             5 S L32-L35
L37             3 S L36 NOT L31
                SEL DN AN L37 2
L38             1 S E1-E3 AND L37
L39             2 S L37 NOT L38
L40             3 S L36 NOT L39
L41            11 S L31,L40
L42            11 S L41 AND L1,L8-L41
L43             2 S L17 AND (?OBESI? OR ?OBESE?)
L44            11 S L42,L43
                E APPETITE/CT
L45             1 S L10 AND E3-E23
                E E3+ALL
L46             1 S L10 AND E2+NT
                E APPETITE/CT
                E E21+ALL
                E E2+ALL
                E E2+ALL
                E EAT/CT
                E E6+ALL
                E ANOREXIA/CT
                E E3+ALL
L47             1 S L10 AND E3,E2+NT
                E BULIM/CT
                E E5+ALL
L48             1 S L10 AND E2
L49             1 S L10 AND (BULIMI? OR ANOREX?)
L50             1 S L45-L49
L51            11 S L44,L50

     FILE 'REGISTRY' ENTERED AT 08:05:20 ON 11 FEB 2004

     FILE 'HCAPLUS' ENTERED AT 08:05:31 ON 11 FEB 2004

     FILE 'EMBASE' ENTERED AT 08:06:17 ON 11 FEB 2004
L52             0 S L7
L53           857 S L9
L54            38 S DEXTRO PHENYLALANYLCYSTEINYLTYROSYL DEXTRO TRYPTOPHYLLYSYLVAL
L55            38 S PHENYLALANYLCYSTEINYLTYROSYL(L)TRYPTOPHYLLYSYLVALYLCYSTEINYLT
L56           885 S L53-L55
                E BODY WEIGHT/CT
                E E3+ALL
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L57        90999 S E11+NT
L58        29685 S E22+NT OR E23+NT
                 E BODY WEIGHT/CT
                 E E6+ALL
L59        62910 S E3+NT
                 E EAT/CT
L60         1542 S E6+NT
                 E E11+ALL
L61        11661 S E4+NT
                 E E11+ALL
L62       174459 S E3+NT
                 E BODY FAT/CT
                 E E3+ALL
L63         9003 S E1
L64           60 S L56 AND L57-L63
                 E ANTIOBES/CT
                 E E6+ALL
L65            0 S E1 AND L56
                 E ANOREX/CT
                 E E5+ALL
L66            8 S E1+NT AND L56
L67            0 S E6+NT AND L56
                 E BULIM/CT
L68            0 S E5-E29 AND L56
                 E E5+ALL
L69           13 S L64,L68 AND PY<=1997
L70            1 S L69 NOT (?TUMOR? OR ?CANCER? OR ?CARCIN?)
L71            0 S L56 AND (CAWTHORNE ? OR LIU Y? OR SENNITT ?)/AU

    FILE 'MEDLINE' ENTERED AT 08:13:28 ON 11 FEB 2004
L72          261 S L7
L73          457 S L9
L74          457 S L72,L73
                 E OBESITY/CT
                 E E3+ALL
L75            1 S L74 AND E60+NT
L76            0 S L74 AND (E70+NT OR E71+NT OR E72+NT OR E74+NT)
                 E BODY WEIGHT/CT
L77            6 S L74 AND (E3+NT OR E26+NT)
L78            1 S L77 AND ?OBES?
                 E EAT/CT
L79            0 S L74 AND (E5+NT OR E10+NT)

    FILE 'MEDLINE' ENTERED AT 08:16:50 ON 11 FEB 2004

    FILE 'BIOSIS' ENTERED AT 08:16:57 ON 11 FEB 2004
L80          481 S L10
L81            0 S L80 AND (CAWTHORNE ? OR LIU Y? OR SENNITT ?)/AU
L82          273 S L80 AND PY<=1998
L83            1 S L82 AND BODY()(WEIGHT OR WT OR MASS)
L84            0 S L82 AND BODY()FAT
L85            3 S L82 AND (WEIGHT OR WT)(L)(GAIN? OR LOSS OR LOSING OR REDUC?)
L86            0 S L82 AND (?OBESE? OR ?OBESI?)
L87            4 S L83,L85
L88            1 S L87 NOT AB/FA

    FILE 'BIOSIS' ENTERED AT 08:20:03 ON 11 FEB 2004

    FILE 'EMBASE' ENTERED AT 08:20:33 ON 11 FEB 2004
L89            3 S L64,L68 AND 1998/PY

    FILE 'HCAPLUS' ENTERED AT 08:21:03 ON 11 FEB 2004
L90           33 S L10 AND (PY<=1998 OR PRY<=1998 OR AY<=1998) NOT L17
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L91             1 S L90 AND L18-L28

     FILE 'WPIX' ENTERED AT 08:22:25 ON 11 FEB 2004
L92            64 S L9/BIX
L93             0 S L55/BIX
                  E LANREOTIDE/DCN
                  E ANGIOPEPTIN/DCN
L94             0 S L92 AND (A61P003-04/IC,ICM,ICS,ICA,ICI OR A61P003:04/ICA)
L95             7 S L92 AND (P731 OR P732 OR P814 OR P816 OR P711)/M0,M1,M2,M3,M4
L96             1 S L92 AND (B14-E12 OR B12-J02 OR B14-E11 OR B12-J01 OR C14-E12
L97             7 S L95,L96
L98             1 S L1
L99           117 S A61K038-31/IC,ICM,ICS
                  E R02073+ALL/DCN
L100          366 S E1 OR 2073/DRN
                  E TRIAL L97
L101          185 S (B04-J10 OR C04-J10)/MC
L102          589 S L92,L99-L101
L103            5 S L102 AND (A61P003-04/IC,ICM,ICS,ICA,ICI OR A61P003:04/ICA)
L104          121 S L102 AND (P731 OR P732 OR P814 OR P816 OR P711)/M0,M1,M2,M3,M
L105           22 S L102 AND P731/M0,M1,M2,M3,M4,M5,M6
L106           22 S L102 AND (B14-E12 OR B12-J02 OR C14-E12 OR C12-J02)/MC
L107           16 S L102 AND (B14-E12 OR C14-E12)/MC
L108            6 S L106 NOT L107
L109           18 S L103,L107
L110           10 S L105 NOT L106-L109
L111           24 S L97,L98,L109
L112           14 S L111 AND (?OBESE? OR ?OBESI?)/BIX
L113           10 S L111 NOT L112
                  SEL DN AN 5
L114            1 S L113 AND E1-E2
L115           15 S L112,L114

     FILE 'WPIX' ENTERED AT 08:48:33 ON 11 FEB 2004

     FILE 'DPCI' ENTERED AT 08:49:29 ON 11 FEB 2004
L116            1 S WO9851331/PN

     FILE 'DPCI' ENTERED AT 08:49:39 ON 11 FEB 2004

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